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INDEX NUMBER

Editors

HOWARD C. TAYLOR, JR. WILLIAM J. DIECKMANN

Official Publication

AMERICAN GYNECOLOGICAL SOCIETY
AMERICAN ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS
CENTRAL ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS
SOCIETY OF OBSTETRICIANS AND GYNAECOLOGISTS OF CANADA
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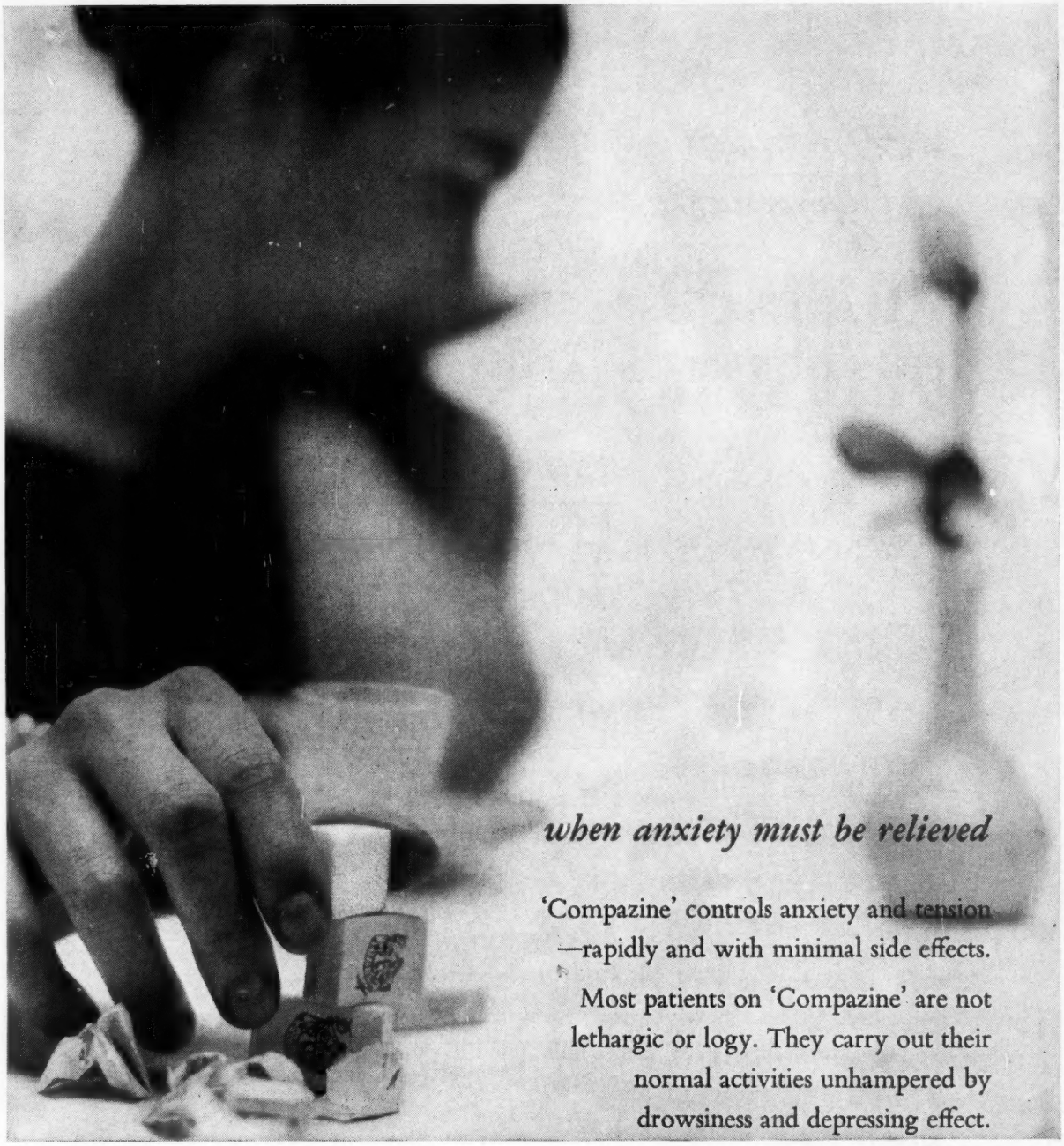

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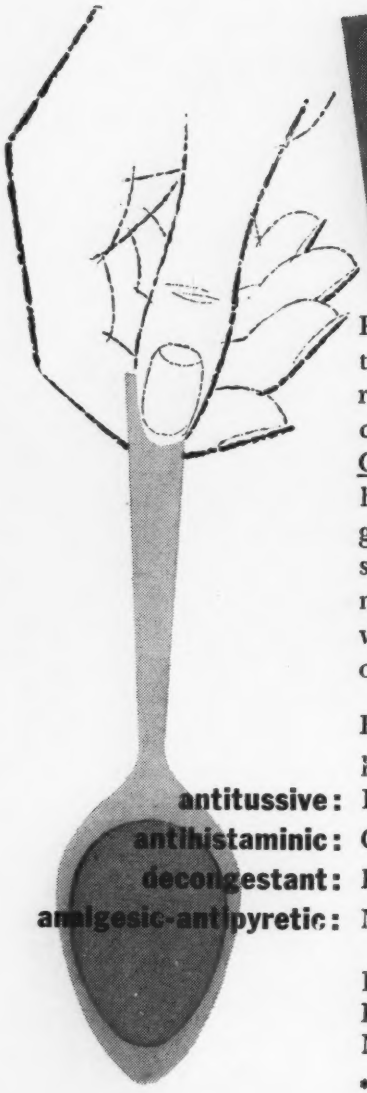

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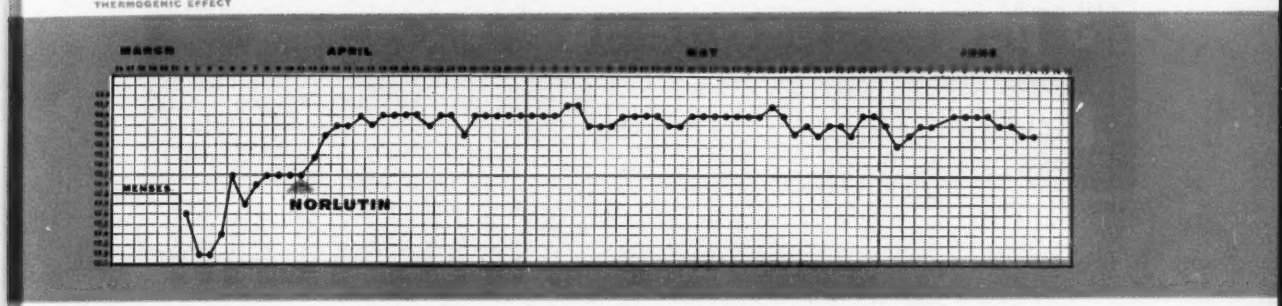

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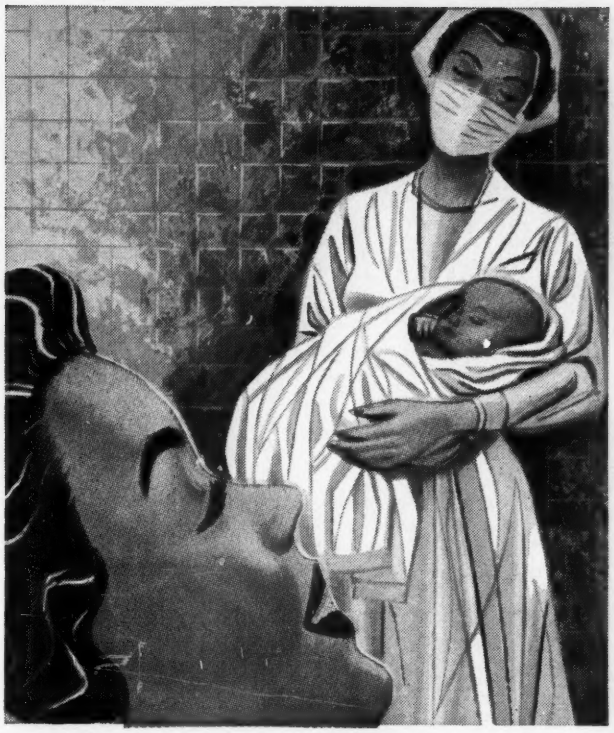

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When narcotics are a standard part of the obstetrical preparation, prophylactic use of NALLINE offers many benefits. Injected five to fifteen minutes before delivery, NALLINE reduces significantly the need for resuscitation and time required for the newborn infant to gasp and cry. In the mother, NALLINE combats narcotic-induced respiratory and circulatory depression and facilitates induction of inhalation anesthesia. NALLINE antagonizes morphine, heroin, methadone, Dromoran®, Levo-Dromoran®, Nisentil®, Dilaudid®, Pantopon®, and Demerol®.

Supplied: In 1-cc. and 2-cc. ampuls (5 mg./cc.). Also, in 1-cc. ampuls (0.2 mg./cc.) for neonatal use. NALLINE comes within the scope of the Federal Narcotic Law.

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DIVISION OF MERCK & CO., INC., PHILADELPHIA 1, PA.

Announcing . . . a new useful dosage form of Equanil

Wyseals*/Equanil®

Wyeth
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Meprobamate, Wyeth

- Especially coated, easy to swallow
- Tranquilizer-conscious patients will not recognize new yellow tablets
- Different from regular 400-mg. and 200-mg. tablets
- Same indications, same dosage as original EQUANIL

NOW YOU HAVE A CHOICE OF 3 EQUANIL TABLETS

WYSEALS EQUANIL, 400 mg.
Yellow tablets, bottles of 50.

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Distinctive, shield-shaped, scored tablets for fine dosage adjustment, bottles of 50.

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Regular, scored, white tablets, bottles of 50.

EPS
EQUANIL®
PHENERGAN® HCl†
SPARINE® HCl‡

—A Wyeth normotropic drug for nearly every patient under stress

*Trademark. †Promethazine Hydrochloride, Wyeth. ‡Promazine Hydrochloride, Wyeth

An established systemic hemostat

adrenosem®
SALICYLATE*

(Brand of carbazochrome salicylate)

effective in virtually every operative procedure

The reports of numerous investigators have established the effectiveness of Adrenosem Salicylate in the control of bleeding. It has been used prophylactically and therapeutically in virtually every operative procedure. Following are some of the procedures and conditions where its usefulness has been demonstrated:

Tonsillectomy, adenoidectomy and nasopharynx surgery
Prostatic, bladder and transurethral surgery
Excessive postpartum bleeding and uterine bleeding
Thoracic surgery
Plastic surgery
Gastrointestinal bleeding

ALSO:
Idiopathic purpura
Epistaxis
Retinal hemorrhage
Hematuria
Hemoptysis
Familial telangiectasia
Pulmonary bleeding
Metrorrhagia and menorrhagia

*U.S. Pat. 2581850; 2506294

THE S. E. MASSENGILL COMPANY
Bristol, Tennessee
New York • Kansas City • San Francisco

One of the many uses of **Adrenosem®**
SALICYLATE

Adrenosem Salicylate is useful in every operative procedure where bleeding and oozing are problems. This hemostatic agent controls blood loss by maintaining normal capillary permeability and by promoting the retraction of severed capillary ends.

One clinician states: "At the recommended dosage levels there are no contraindications. Patients treated for more than two years show no toxic effects attributable to the drug."[1]

Adrenosem Salicylate is supplied in

Ampuls
Tablets
and as a Syrup

1. Riddle, A.C., Jr.: Adrenosem Salicylate: A Systemic Hemostat, Oral Surg., Oral Med., Oral Path. 6:617 (June, 1955).

Vaginal hysterectomy.
Without Adrenosem. Note bloody field.

Vaginal hysterectomy.
With Adrenosem. Note dry field.

Write for comprehensive illustrated brochure describing the action and uses of Adrenosem Salicylate.

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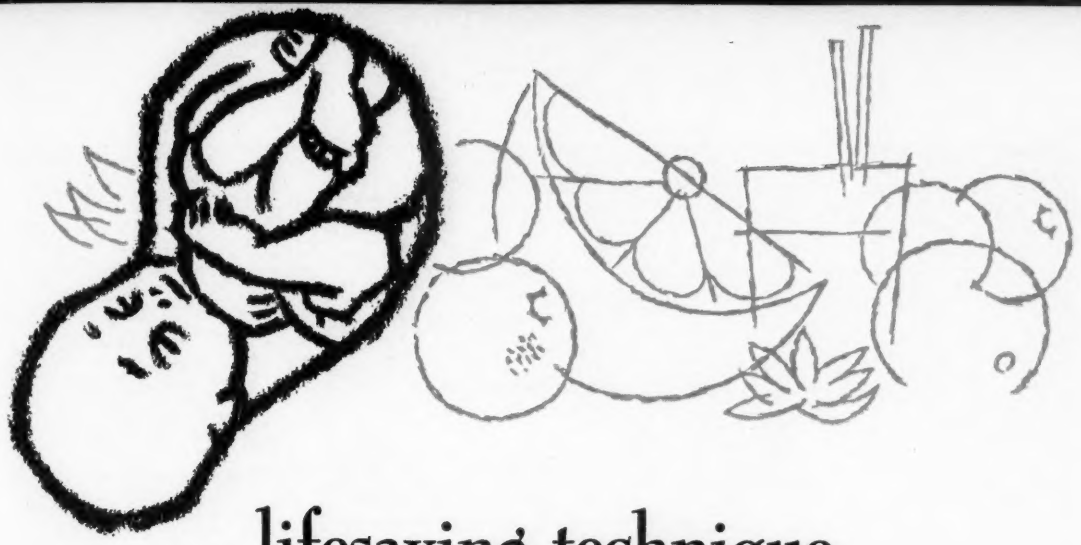


lifesaving technique for the unborn *includes* high citrus intake

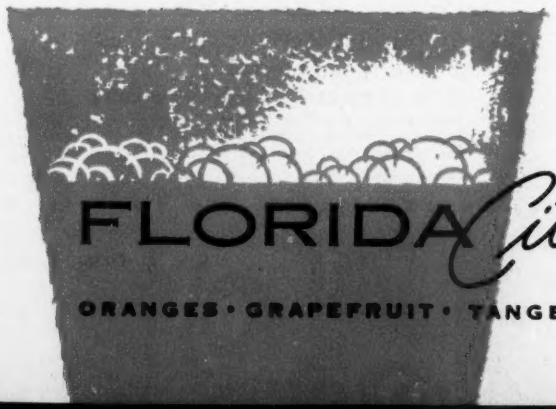
Abortion-prone mothers deliver live babies in nearly 9 out of 10 pregnancies

Reporting on 134 pregnancies in 100 habitual abortion patients, Javert* describes a management program that resulted in live deliveries in all but 16 pregnancies. The previous 95.2 per cent rate of spontaneous abortions was reduced to 11.9 per cent by his comprehensive regimen which includes a high citrus intake (supplying up to 350 mg. of vitamin C daily), supplemented by 150 mg. of ascorbic acid and 5 mg. of vitamin K daily. Javert believes these antihemorrhagic vitamins "serve as a 'never-leak' . . . keeping physiologic decidual hemorrhage from becoming pathologic."

AVERAGE CITRUS INTAKE TO SUPPLY 350 MG. VITAMIN C DAILY

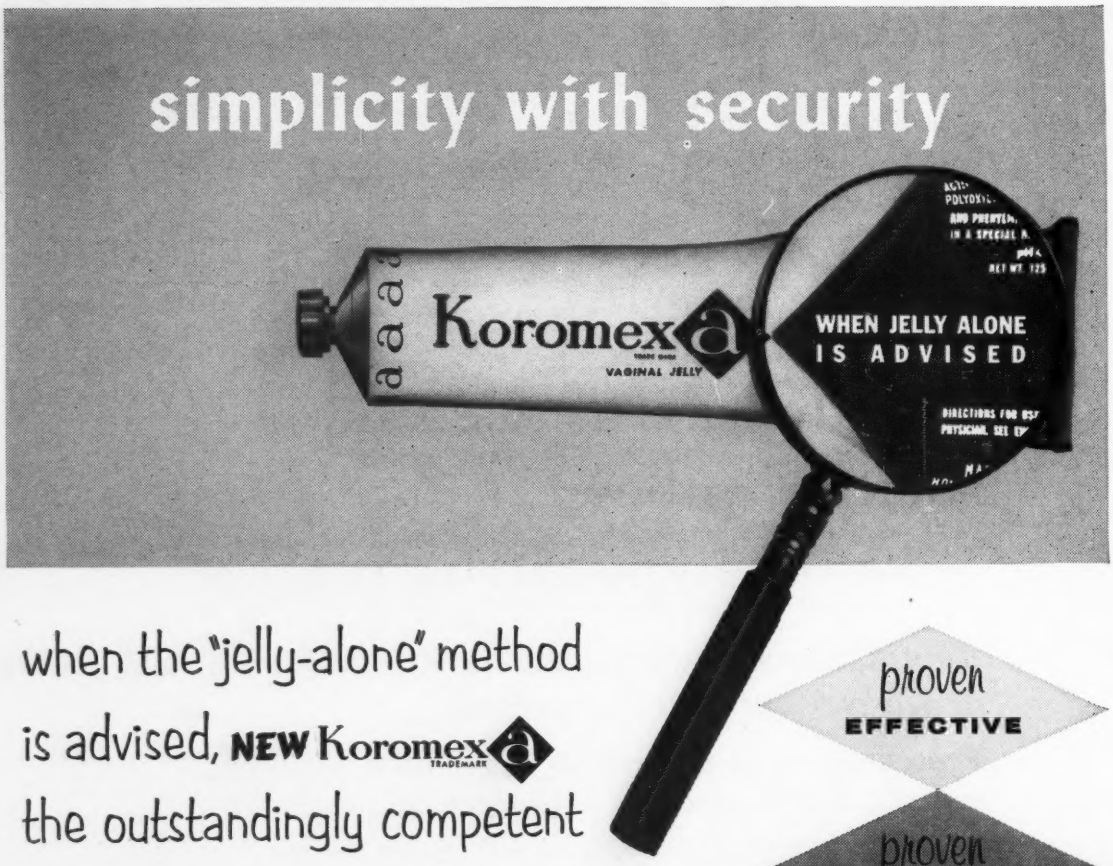
28 oz. orange or grapefruit juice	**or**	1 grapefruit 2 oranges 2 tangerines	**or**	½ grapefruit 1 orange 16 oz. orange juice

Florida Citrus Commission, *Lakeland, Florida*



*Javert, C. T.: Obst. & Gynec. 3:420, 1954; *Cf.* Greenblatt, R. B.: Obst. & Gynec. 2:530, 1953.

simplicity with security



when the "jelly-alone" method is advised, **NEW** Koromex® the outstandingly competent spermatocidic agent.....is now available to physicians.

proven **EFFECTIVE**

proven **RELIABLE**

proven **STABLE**

proven **ACCEPTABLE**

The beautiful zippered plastic kit — originated by H-R — the modern way to store the jelly and the applicator.

availability, another H-R "first"...

Large tube of **Koromex** vaginal jelly, 125 grams, with patented measured dose applicator, is supplied in a washable, appealingly feminine zippered kit, at no extra charge, for home storage.

The 125 gram tube of **Koromex®** may also be bought separately at any time.

Factual literature sent upon request.

active ingredients:
in a special barrier type base

Boric Acid	2.0%
Polyoxyethylenenonylphenol	0.5%
Phenylmercuric Acetate	0.02%

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optimum response

in corticosteroid therapy with

PARACORT*

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PARACORTOL*

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supplied: PARACORT and PARACORTOL are available as 5-mg. and 2.5-mg. scored tablets; bottles of 30 and 100.

THREE TO FIVE TIMES THE ACTIVITY OF CORTISONE OR HYDROCORTISONE

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a preferred route to follow in topical anesthesia

Tronothane®

(*Pramoxine, Abbott*)

Puts safety first while relieving your patient's pain and itching.
More than 15,600 case studies showed negligible sensitization and no toxicity was observed.

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'Thorazine' reduces the need for resuscitation . . .

	'THORAZINE' GROUP		CONTROL GROUP	
anesthetic	Spinal	General	Spinal	General
patients	118	17	105	45
mild resuscitation (oxygen by face mask)	6.8%	17.7%	13.3%	31.0%
active resuscitation (aspiration with tracheal catheter; oxygen via catheter or positive pressure resuscitation apparatus)	none	none	1.9%	6.7%
total	6.8%	17.7%	15.2%	37.7%

The above chart shows the significant decrease—more than half—in the incidence of narcotized and apneic infants obtained by Anz and Smith[1] following their use of 'Thorazine'-potentiated analgesia. (Further information available on request.)

1. Anz, U.E., and Smith, L.J.: Am. J. Obst. & Gynec. *71*:1242 (June) 1956.

THORAZINE*

chlorpromazine, S.K.F.

one of the fundamental drugs in medicine

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NEW!

'THORAZINE' SPANSULE†

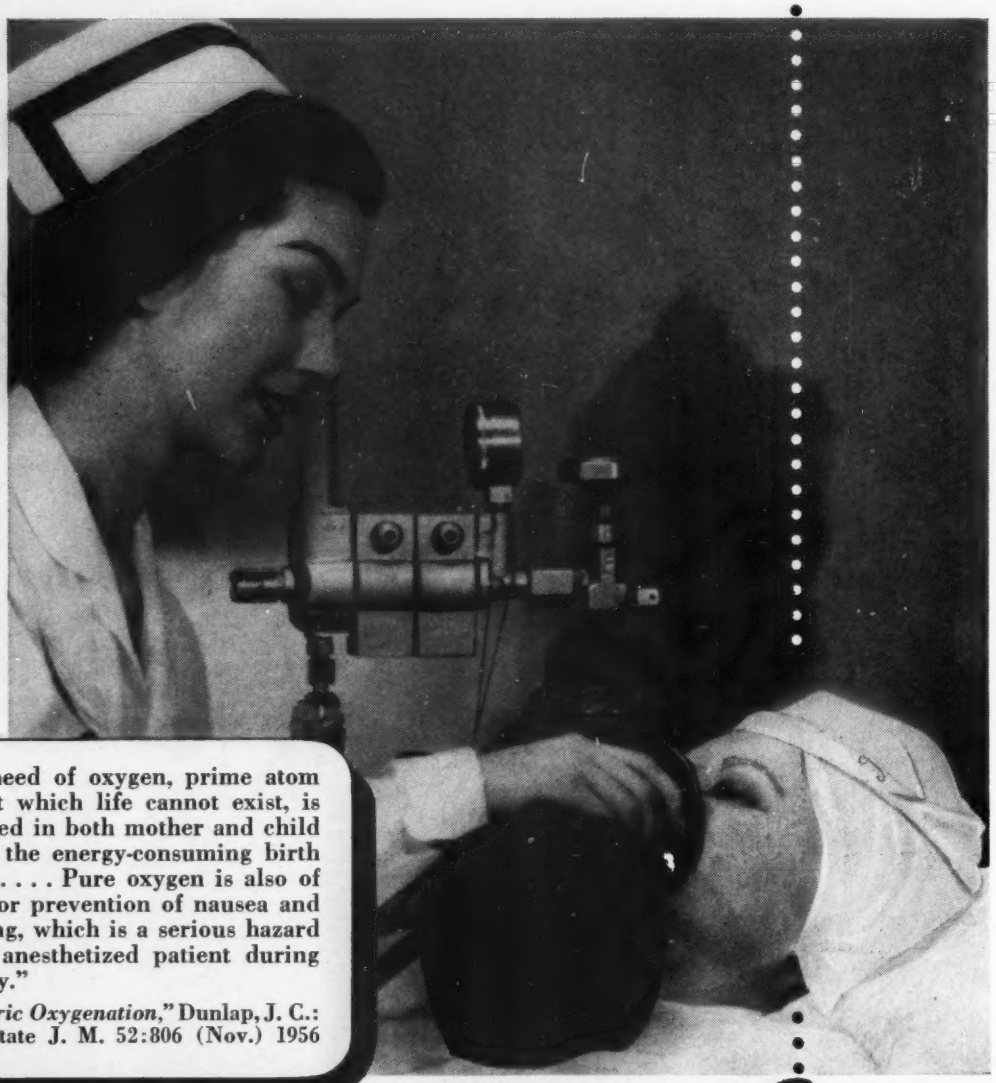
capsules

offering all-day or all-night 'Thorazine' therapy with a single oral dose.

Available in four strengths: 30 mg., 75 mg., 150 mg. and 200 mg.

*T.M. Reg. U.S. Pat. Off.
†T.M. Reg. U.S. Pat. Off. for sustained release capsules, S.K.F.

Before and during delivery ..... O_2



"The need of oxygen, prime atom without which life cannot exist, is increased in both mother and child during the energy-consuming birth process. . . . Pure oxygen is also of value for prevention of nausea and vomiting, which is a serious hazard to the anesthetized patient during delivery."

"Obstetric Oxygenation," Dunlap, J. C.: Texas State J. M. 52:806 (Nov.) 1956

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will her arms be filled this time?

Improve your abortion-prone patient's chance of coming to term by creating optimal conditions for the maintenance of pregnancy with Nugestoral. Nugestoral supplies five agents known to contribute to fetal salvage. Taken in a dose of three tablets per day, Nugestoral will help bring your abortion-prone patients to term.

new *for the abortion-prone patient*

NUGESTORAL®

Each tablet contains ethisterone (Progestoral®), 15 mg; hesperidin complex, 175 mg; ascorbic acid, 175 mg; sodium menadiol diphosphate (vitamin K analogue), 2.0 mg; dl, alpha-tocopherol acetate, 3.5 mg. In packages of 30 tablets.

ORGANON INC. *Orange, New Jersey*

...one thing bothers me about leaving the hospital. My milk is just starting. Suppose, in the excitement of going home, I don't have enough milk and the baby goes hungry?...

for the early "stand-by" bottle...

SIMILAC®

as the compatible supplement

Feeling at home

During the first days at home with her new baby, the mother may find her milk supply is low, from excitement and nervousness in the face of readjustments she must make at home. You can reassure her that Similac is closely equivalent to her own milk, and that breast feedings and Similac feedings are compatibly alternated.

A natural compatible supplement

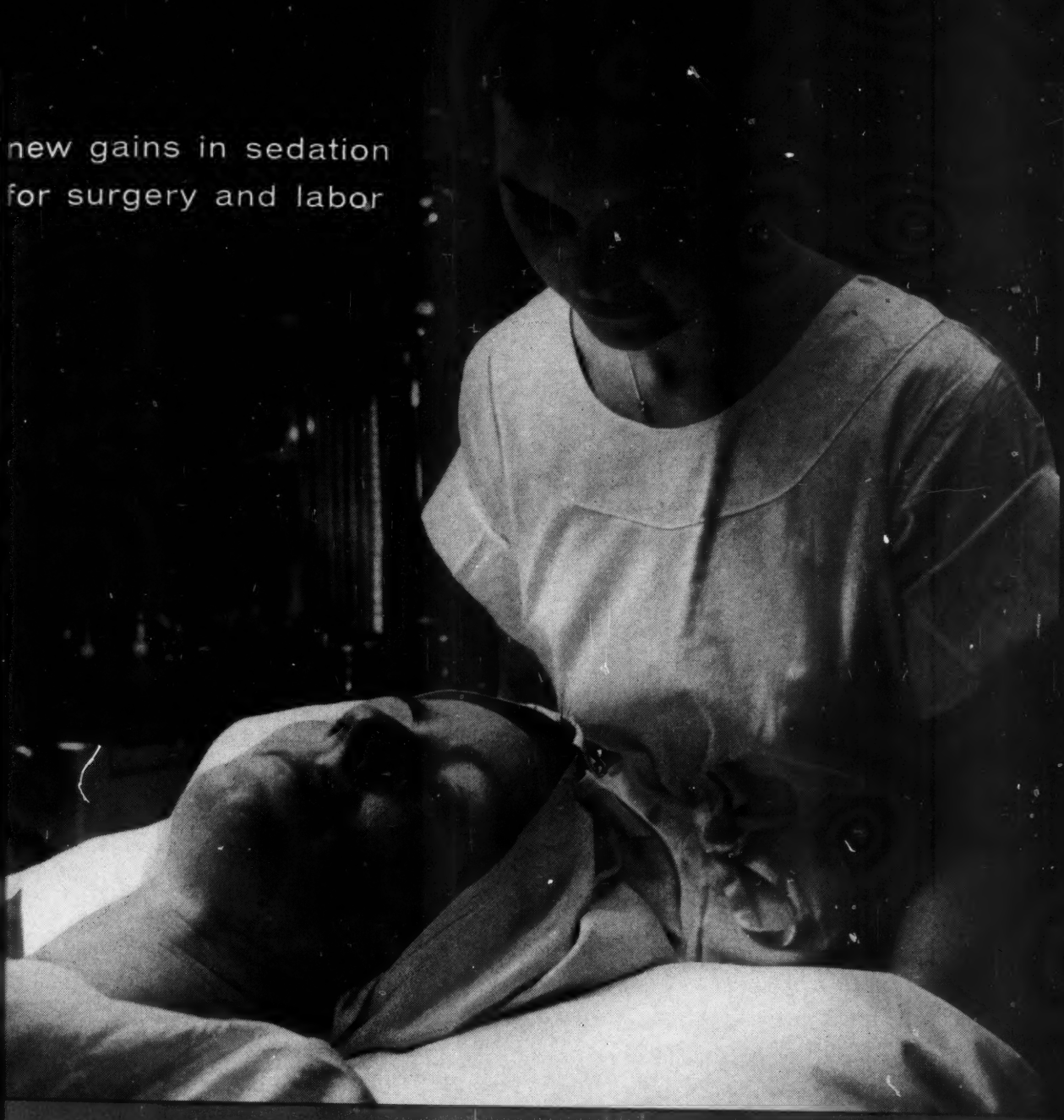
Similac provides a natural and logical supplement to breast milk. Physiologic levels of essential fatty acids, protein and carbohydrate in the same balanced proportion as in breast milk, plus all known essential vitamins are provided in the formula.

With the reassurance that her infant will not want for good nutrition, the breast-feeding mother may feel more confident and at ease in the early feeding situation. The tensions of readjustment may be more easily and confidently met with reliance on Similac for the "stand-by" bottle. This reassurance even may help her nurse the baby longer.

Compatible infant feeding . . .
breast feeding and Similac

RESEARCH SERVICE NUTRITION Ross

ROSS LABORATORIES,
Columbus 16, Ohio



QUIESCENCE

. . . not depression

1. Relieves apprehension without blocking perception or depressing the vital functions
2. Promotes composure and cooperation
3. Induces light sleep with easy awakening
4. Controls nausea and vomiting both prophylactically and therapeutically
5. Reduces analgesic and sedative requirements

Comprehensive literature is available on request.

Wyeth®
Philadelphia 1, Pa.

PHENERGAN®
HYDROCHLORIDE
Promethazine Hydrochloride

INJECTION
TABLETS
SUPPOSITORIES

extra protection for every conception

Decidual bleeding due to capillary fragility leads to abortion

Hesper-C Prenatal

with capillary-protective factors plus vitamins-minerals

a precaution in every pregnancy
a necessity in habitual abortion[1,2]

Routine care during pregnancy should include protection against decidual bleeding. To guard against spontaneous and habitual abortion, Hesper-C Prenatal provides the essential capillary-protective factors (hesperidin complex and ascorbic acid) *plus* the supplemental vitamins and minerals required during gestation.

The usual daily dosage (2 capsules t.i.d.) provides:			
HESPERIDIN COMPLEX	600 mg.	Thiamine Mononitrate	7.5 mg.
ASCORBIC ACID	600 mg.	Riboflavin	4.5 mg.
Ferrous Gluconate (15 mg. iron)	130 mg.	Nicotinamide	30.0 mg.
Calcium Pantothenate	6 mg.	Vitamin B_{12}	4.5 mcg.
Calcium Carbonate (500 mg. calcium)	1.25 Gm.	Folic Acid	0.3 mg.
Vitamin A Acetate	6,000 U.S.P. Units	Pyridoxine Hydrochloride	10.0 mg.
Vitamin D_2	1,200 U.S.P. Units	Copper Sulfate (3.0 mg. copper)	12.0 mg.
		Potassium Iodide (0.3 mg. iodine)	0.4 mg.

Providing the daily requirements or more of vitamins and iron during pregnancy as recommended by the National Research Council.

1. Greenblatt, R. B.: Obst. & Gynec. *2*:530, 1953.
2. Dill, L. V.: M. Ann. District of Columbia *23*:667, 1954.

THE NATIONAL DRUG COMPANY
Philadelphia 44, Pa.

Products of Original Research

HCP 1800/57

Bactericidal! Fungicidal!

DERMOPLAST® aerosol

TOPICAL ANESTHETIC • ANTIPRURITIC • ASTRINGENT

IN OBS & GYN USE

NEW—3 OZ.
PRESCRIPTION SIZE

for individual therapy in hospital and home.

Also available in . . .
HOSPITAL economy size .... 12 oz.
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PROVIDES NEW RELIEF OF SURFACE PAIN AND ITCHING ON CONTACT WITHOUT TOUCHING AFFECTED AREAS

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hemorrhoids
pruritus ani
pruritus vulvae
wounds
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FORMULA: benzocaine 4.7%; benzethonium chloride 0.1%; menthol 0.5%; dissolved in oils (Doho process)

Substantiating clinical data sent on request

MALLON DIVISION
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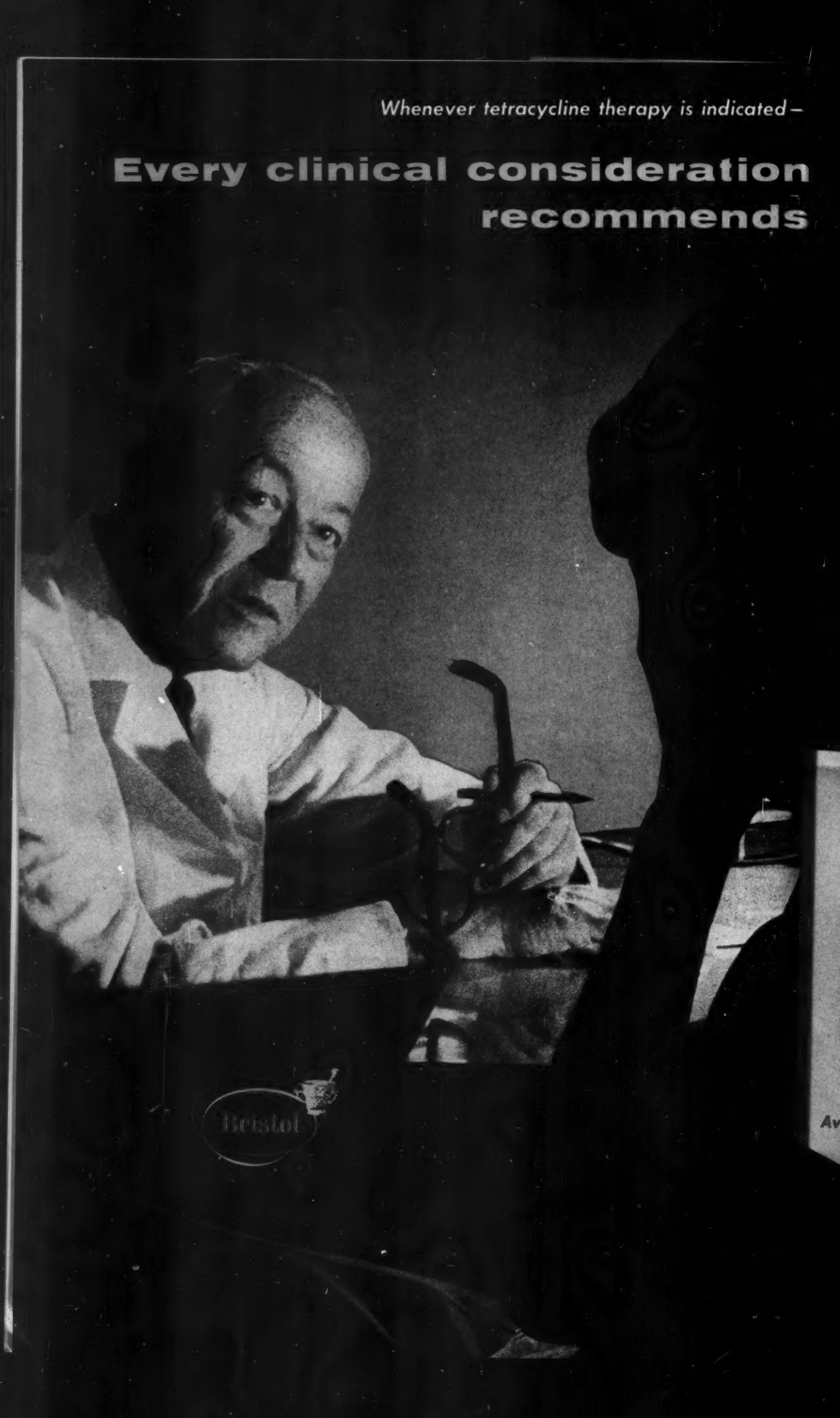
100 VARICK ST.
NEW YORK 13, N.Y.

Whenever tetracycline therapy is indicated –

Every clinical consideration recommends



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THE ORIGINAL TETRACYCLINE PHOSPHATE COMPLEX

U S PAT NO 2,701,600

for faster, more certain control of infection

- A single, pure drug (not a mixture)
- High tetracycline blood levels
- Clinically "sodium-free"
- Equally effective, b.i.d. or q.i.d.
- Exceptionally free from adverse reactions
- Dosage forms for every therapeutic need

BRISTOL LABORATORIES INC., SYRACUSE, NEW YORK

Available for your prescription at all leading pharmacies

Estrogen-androgen therapy effectively prevents postpartum breast engorgement

Satisfactory results were obtained in over 96 per cent of cases in a series of 267 patients who received estrogen and androgen as combined in "Premarin" with Methyltestosterone. Therapy was started as soon as possible after delivery. No untoward side effects were noted. In addition, the absence of mental depression in the puerperium was considered of notable importance.*

*Fiskio, P. W.: GP *11*:70 (May) 1955.

"PREMARIN"® with METHYLTESTOSTERONE

for combined estrogen-androgen therapy

Ayerst Laboratories • New York, N. Y. • Montreal, Canada

5648

In urinary-tract infections

HIGH TISSUE LEVELS

HIGH BLOOD LEVELS

LOW TOXICITY

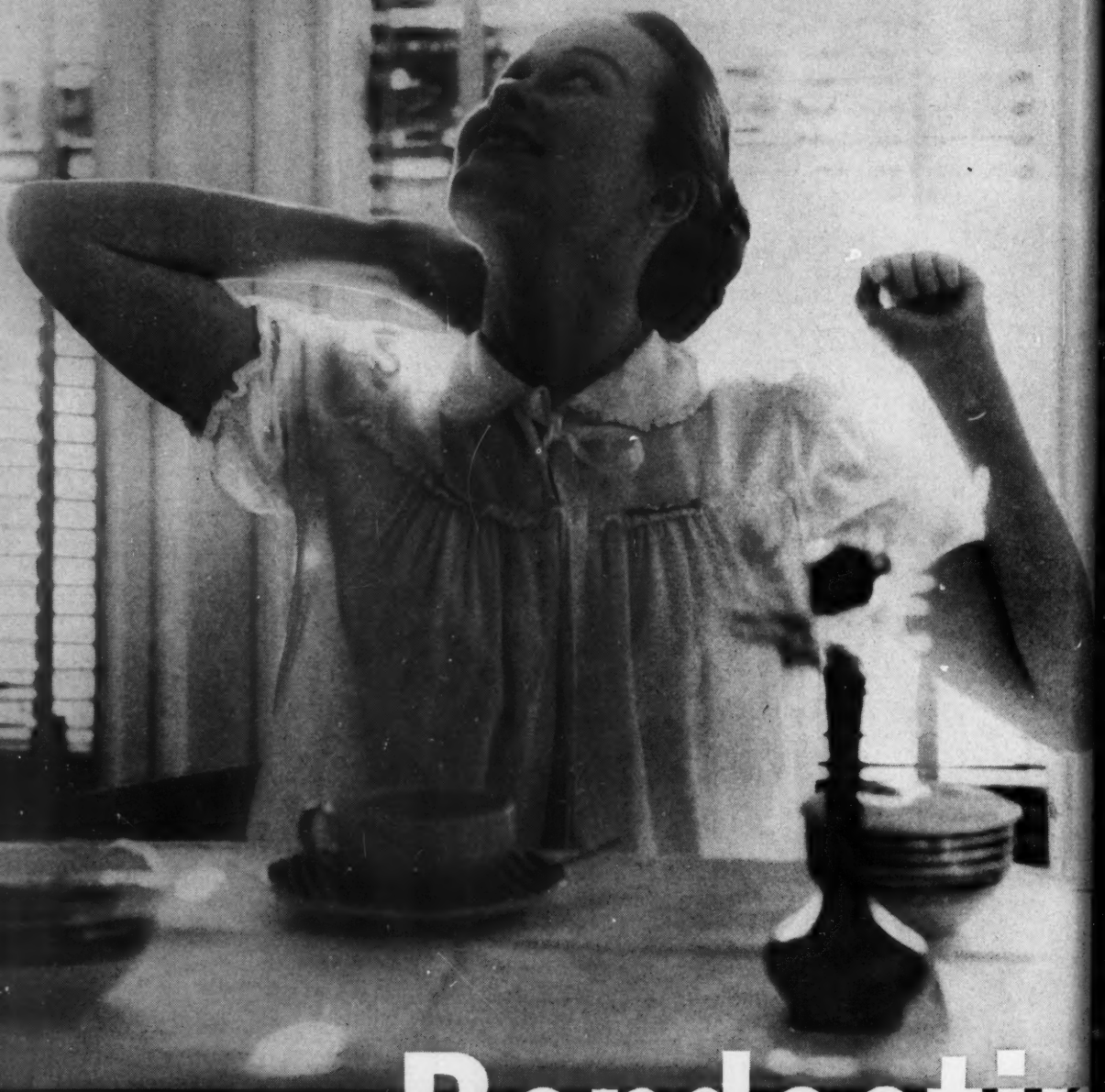
Wyeth®
Philadelphia 1, Pa.

SUSPENSION TABLETS

SULFOSE®

Trisulfapyrimidines, Wyeth
(Sulfadiazine, Sulfamerazine, Sulfamethazine)

treat her morning sickness... the night befor



in 941 cases[1,2] effective in all but 17

Bendectin

2 tabs. h.s.

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New York • CINCINNATI • St. Thomas, Ontario
Another Exclusive Product of Original Merrell Research

1. Nulsen, R. O.: Ohio State M. J. 53:665, 1957.
2. Clinical communications, 1956-57.

setting new standards
ETHICON®
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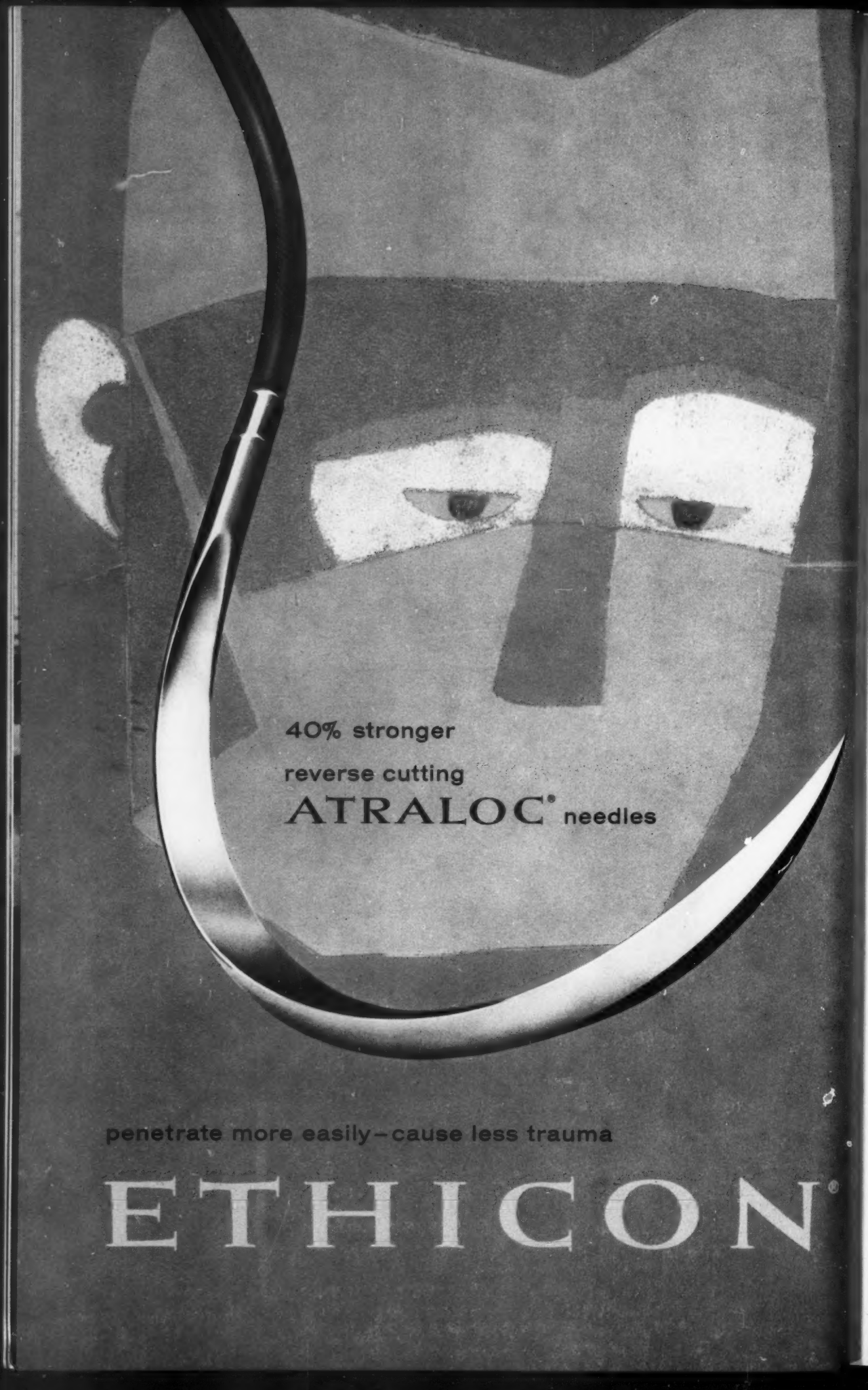
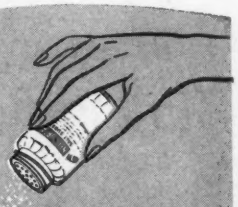

40% stronger
reverse cutting
ATRALOC® needles
penetrate more easily–cause less trauma
ETHICON®

During Pregnancy

SALT *without* SODIUM

WATER RETENTION (excessive gain in weight—pitting edema) is quite common in pregnancy. Sodium, particularly if used excessively, may accelerate this process. Conversely, sodium restriction can prevent excessive water retention.



SALT *WITHOUT* SODIUM

New **IMPROVED**

NEOCURTASAL®

AN EXCELLENT SALT REPLACEMENT

for

"Salt-Free" (Low Sodium) Diets

Tastes, Looks, Pours, Used **LIKE SALT**

Contains potassium chloride, potassium glutamate, glutamic acid, calcium silicate, potassium iodide (0.01%).

Assures patient cooperation

2 oz. shakers and 8 oz. bottles

Sold Only Through Drugstores.

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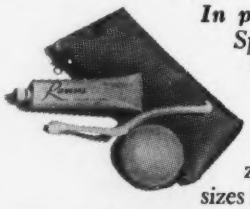
Wanted: CHILDREN
Today's families are planned big

THE earlier phase of the baby boom, characterized by its sharp rise in first and second births, is being sustained by the "unusually large numbers of children born in established families."[1] *Almost one-third of the 1956 babies were third or fourth children* – a higher proportion "than for any year since before World War I."

Big, but spaced families – Many of these children will have one, two or even more brothers or sisters, especially in upper-class families. A survey recently completed among 29,494 graduates of 178 colleges shows that the men of the class of '45 have families *averaging 70% larger* than the men of the class of '36 in the ten years after graduation.[2]

Ideal method for family planners – When prudent young wives ask advice to help them space their children, they want to be sure the method recommended really provides protection. You can give them this assurance with the diaphragm-jelly technique, *the preferred method for women of high parity*. Adopted by parenthood clinics "as possessing the least degree of fallibility,"[3] this dependable method reduces "the likelihood of conception by at least 98 per cent."[4]

Comfort and security – RAMSES® Diaphragm and Jelly offer comfort for the patient as well as the peace of mind that comes with the use of a reliable technique. The smooth, cushioned rim of the RAMSES Diaphragm prevents irritation. Its flexibility in all planes permits complete freedom of movement. RAMSES Jelly,* a "10-hour" jelly because it occludes for that long, quickly immobilizes sperm and is safe for continued use. Wives who want their families *when* they want them are confident that you have given sound advice when you tell them that for more than 30 years physicians have relied on RAMSES protection in family planning.



In prescribing a diaphragm – *Specify the attractive, complete unit – RAMSES "TUK-A-WAY"® Kit #701 with diaphragm, introducer, and 3 oz. tube of jelly in a washable, zippered bag. Diaphragm in sizes from 50 to 95 mm. Additional jelly, in 3 and 5 oz. tubes, at all pharmacies.*

References: 1. Statist. Bull. Metrop. Life Insur. Co. 38:6 (March) 1957. 2. College Study Report: Population Bull. *11*:45 (June) 1955. 3. Novak, E., and Novak, E. R.: Textbook of Gynecology, Baltimore, The Williams & Wilkins Co., 1956. 4. Tietze, C.: Proc. 3rd Internat. Conf., Planned Parenthood, 1953.

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*Active agent, dodecaethyleneglycol monolaurate 5%, in a base of long-lasting barrier effectiveness.

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FOR YOUR PATIENTS WITH MUSCULOSKELETAL PAIN

a **NEW** oral analgesic compound for moderate to moderately severe pain

Zactirin*

Ethoheptazine Citrate with Acetylsalicylic Acid, Wyeth

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Wyeth

EFFICIENTLY

ANALGESIC

SAFELY

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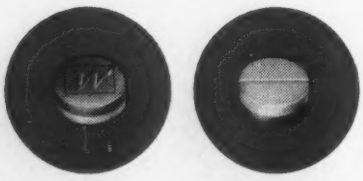
A NEW ANALGESIC FOR MUSCULOSKELETAL PAI

ENTIRELY **NEW** DOSE FORM: 2-layer tablet

COMPARABLE TO **CODEINE** IN POTENCY:

2 Zactirin

TABLETS are equivalent in potency to ½ grain of codeine plus 10 grains of acetylsalicylic acid



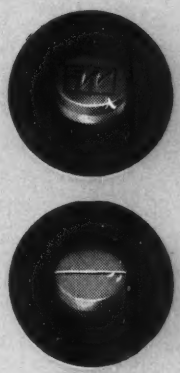
POTENTLY **ANALGESIC**

SAFELY **NON-NARCOTIC**

EFFECTIVELY **ANTI-INFLAMMATORY**

In the field of moderate to moderately severe pain, ZACTIRIN establishes a new concept in analgesia—effective pain control by mouth without resort to narcotic drugs. ZACTIRIN contains ethoheptazine citrate, the culmination of original Wyeth research for pure, potent analgesic action without the liabilities of codeine. For anti-inflammatory action, ZACTIRIN contains acetylsalicylic acid.

Totally, ZACTIRIN has an analgesic and anti-inflammatory effectiveness comparable to that of codeine plus acetylsalicylic acid. ZACTIRIN has a high degree of toleration. It is free of codeine's side-effects, free of addiction liability, free of appreciable drug tolerance.



Zactirin*

Ethoheptazine Citrate with Acetylsalicylic Acid, Wyeth

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Wyeth®
Philadelphia 1, Pa.

for moderate to moderately severe musculoskeletal pain

the effectiveness of codeine plus acetylsalicylic acid

- Low-back pain
- Pain of bursitis, synovitis, and related conditions
- Minor traumatic pain
- Subacute postoperative pain
- Postpartum abdominal or perineal pain

Supplied: Distinctive, 2-layer yellow-and-green tablets, bottles of 48. Each tablet contains 75 mg. of ethoheptazine citrate and 325 mg. (5 grains) of acetylsalicylic acid.

Comprehensive literature available on request

Simplified Oral Treatment *of* Menstrual Irregularities

Duosterone®

anhydrohydroxyprogesterone 10.00 mg.
primed by ethinyl estradiol 0.01 mg.
} per tablet

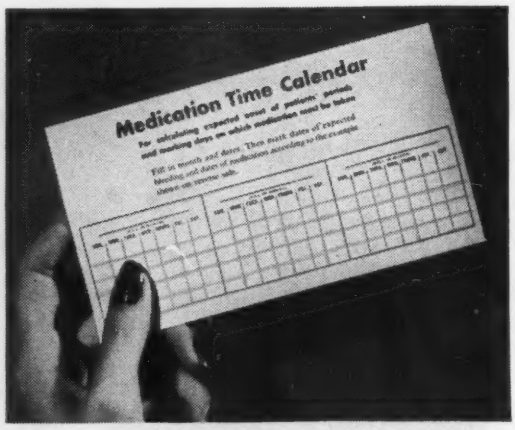
Dysfunctional uterine bleeding
Secondary amenorrhea

Given by mouth for five days, DUOSTERONE® tablets simulate the hormonal requirement of the secretory phase of the menstrual cycle. Normal menstrual function thus may be *safely* and conveniently restored with twin-hormone action of DUOSTERONE: oral progesterone primed with ethinyl estradiol. Normal menses may be set off by DUOSTERONE, much as touching the pendulum starts a wound clock. According to the concept of Holmstrom[1], DUOSTERONE therapy may initiate an endocrine chain-reaction resulting in spontaneous ovulatory cycles.

Other indications: Habitual or threatened abortion and functional sterility have also responded to DUOSTERONE therapy.

Supplied: DUOSTERONE tablets in bottles of 25 and 100, on prescription only.

1. Amer. J. Obst. & Gynec., 68:1321, 1954.



Write for:

Medication Time Calendar
and clinical supplies
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Roussel — ROUSSEL CORPORATION • 155 East 44th St., New York 17, N.Y.

eliminate pain...while maintaining muscle relaxation and patient cooperation . . . **in obstetrical delivery**

Saddle block with Heavy Solution Nupercaine, testified safe by hundreds of thousands of successful deliveries, fulfills the criteria for ideal obstetrical anesthesia: "*1. An anesthetic that is safe for both mother and baby. 2. An anesthetic that is easy to administer, and one in which personnel can be quickly and easily trained. 3. An anesthetic which alleviates pain of delivery for the patient while still inducing complete relaxation for the benefit of the obstetrician.*"[1]

1. Seegar, J.K.B.E., and Devlin, A.J.: Maryland M.J. 5:330 (June) 1956.

Supplied: 1:400 Nupercaine hydrochloride in 5% dextrose, 2-ml. ampuls, each ml. containing 2.5 mg. Nupercaine and 50 mg. dextrose; cartons of 10.

HEAVY SOLUTION **Nupercaine®**
hydrochloride
(dibucaine hydrochloride with dextrose 5% CIBA)

CIBA
SUMMIT, N. J.

2/2379HS

Keep the "reducer" happy

'METHEDRINE'®

in OBESITY

means help

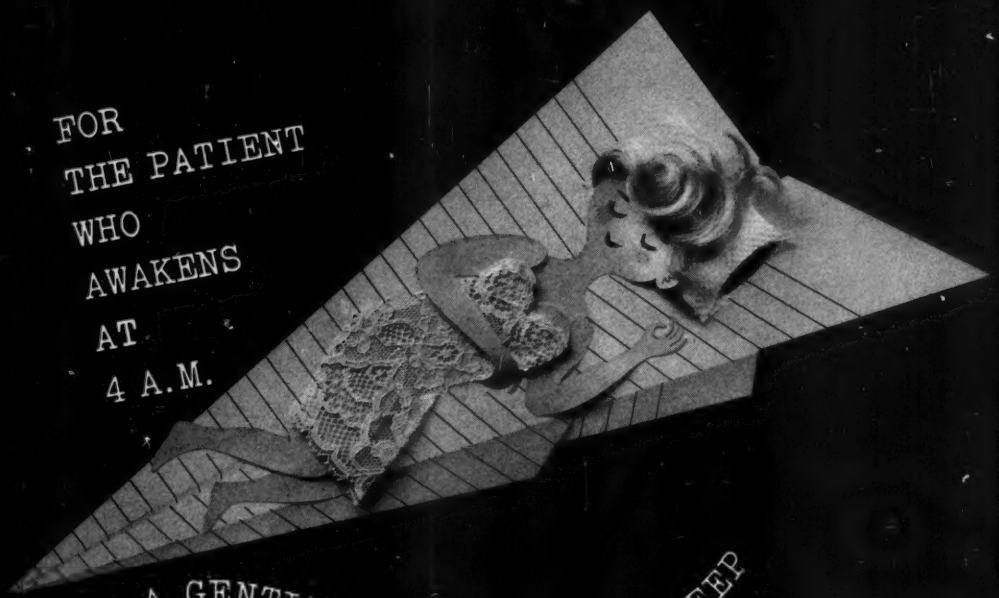
- For those who eat too much
- For those who are depressed

'Methedrine' dispels abnormal craving for food, subtly elevates the mood.

'Methedrine'® brand Methamphetamine Hydrochloride Tablets 5 mg., scored

BURROUGHS WELLCOME & CO. (U. S. A.) INC., Tuckahoe, New York

FOR
THE PATIENT
WHO
AWAKENS
AT
4 A.M.



A GENTLE GLIDE BACK TO SLEEP

AND
AN ALERT
AWAKENING
AT THE DESIRED HOUR

NOLUDAR®

NOLUDAR® 'Roche'

methyprylon

- At bedtime or for pre-dawn insomnia
- Non-barbiturate, non-habit forming
- No morning mental haze
  a ringing telephone or alarm clock
  easily rouses the patient
  at any time during sleep.
- Broad safety margin
- The physician's personal hypnotic
  Noludar is advantageous when it is
  necessary to answer the telephone
  or go on a call at night.

DOSAGE:

two 200 mg tablets gently but firmly
put the confirmed insomniac to sleep.

one 200 mg tablet lulls the geriatric
or pediatric patient to sleep.

one 50 mg tablet t.i.d. provides
daytime sedation without drowsiness.

Roche Laboratories
Division of Hoffmann-La Roche Inc.
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A brighter "Good morning, doctor!"

No complaints about

* post-episiotomy,
* tender hemorrhoids,
* or fissured nipples when you prescribe

Americaine® Topical Anesthetic

Americaine relieves surface discomfort quickly, sustains relief up to six hours with a single application—because only Americaine contains 20% dissolved benzocaine.

What about sensitivities? None reported in over 11,800 published clinical cases[1]...negligible incidence in 10 years' steadily growing use.

Americaine Aerosol

For quick spray application. Available in 3 oz. prescription size, and 5.5 oz. and 11 oz. dispensers.

Americaine Ointment

For simple manual application. Available in 1 oz. tube w/applicator.

1. References on request.

ARNAR-STONE LABORATORIES, INC., *Mount Prospect, Ill.*

the NEW Softab*

for
nausea and vomiting
of pregnancy

motion sickness • inner-ear disturbances

SOFTAB FORM

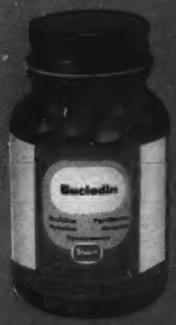
Bucladin

pleasant-tasting Softab*
melts quickly in the mouth—
no water needed
attacks basic causes centrally
and peripherally
contains *both* antiemetic
and antispasmodic
longer acting—lower in cost

Each Softab contains:

Buclizine Hydrochloride	50 mg.
Vitamin B$_{12}$	10 mg.
Scopolamine (Hyoscine) HBr	0.2 mg.
Atropine Sulfate	0.05 mg.
Hyoscyamine Sulfate	0.05 mg.

Write for samples and literature



Stuart

THE STUART COMPANY
PASADENA, CALIFORNIA

*TM/PAT. PEND.

superior vulvovaginal therapy

with

trichotine®

a surface-active detergent
which dissolves the viscid film

a bactericide and fungicide
which penetrates and destroys the microorganisms

an antipruritic
for prompt relief from itching and discomfort

a psychic and aesthetic adjunct
providing an immediate sense of well-being

Indications:

Vaginitis and Vulvovaginitis – nonspecific, trichomonal, monilial, senile, diabetic, postoperative

Cervicitis – subacute and chronic

Pruritus Vulvae – hot pack applications

Office Clean-up – concentrated solutions

Hygienic Irrigations – postcoital, postmenstrual

suggestion:

Upon retiring, a TRICHOTINE douche followed by a VACID suppository provides maximum effectiveness and 24-hour pH control.

The TRICHOTINE formula contains sodium lauryl sulfate, sodium perborate, sodium borate, thymol, menthol, eucalyptol and methyl salicylate.

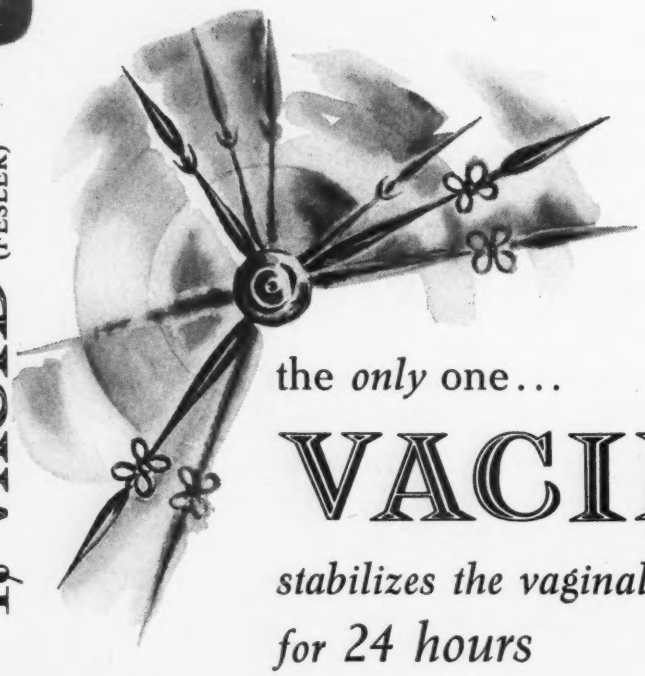
samples and literature upon request.

The Fesler Co., Inc.

375 Fairfield Ave. Stamford, Conn.

℞ trichotine (FESLER)

℞ VACID (FESLER)



the *only* one...

VACID®

stabilizes the vaginal pH for 24 hours

Extensive clinical experience demonstrates the therapeutic value of the continual maintenance of the normal physiologic pH in the treatment of trichomonal, monilial, and non-specific bacterial infections and in cervicitis.

Only Vacid provides a high capacity cationic exchange resin accurately buffered to stabilize the vaginal pH range at 4.0-4.5 for twenty-four hours.

Indications: **IN VAGINITIS** – trichomonal, monilial, non-specific

CERVICITIS – subacute and chronic, including eversions

POSTCAUTERY and **POSTCONIZATION**

PREGNANCY and **POSTPARTUM** – prophylactically and in infections.

Suggestion: Upon retiring, a Vacid suppository preceded by a Trichotine douche provides maximum effectiveness and 24-hour pH control.

FORMULA – Each Vacid suppository contains a high capacity polyacrylic cationic exchange resin (activated and buffered) combined with lactose.

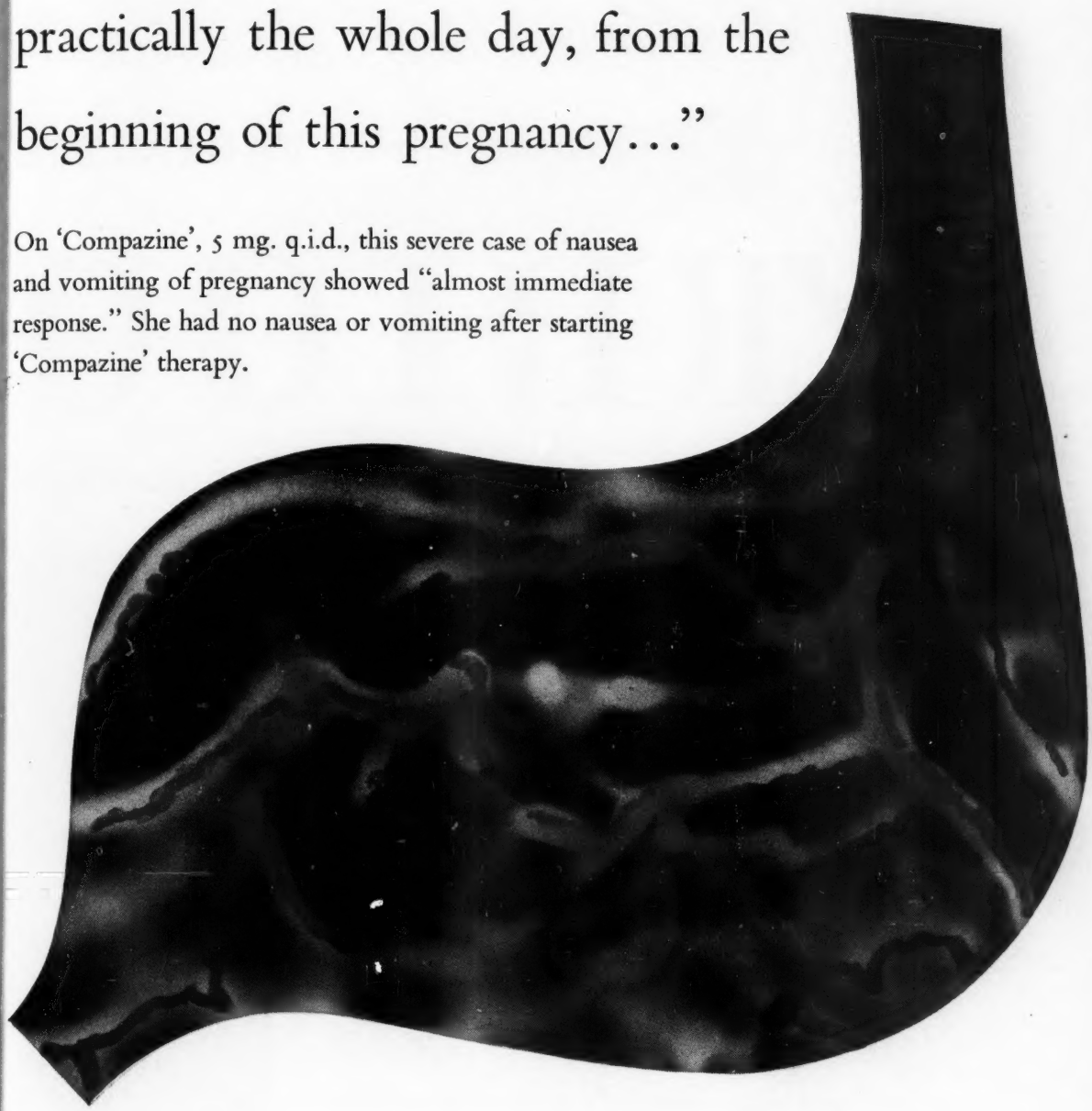
samples and literature upon request

The Fesler Co., Inc.

375 Fairfield Ave. Stamford, Conn.

"...nauseated and vomiting every day, practically the whole day, from the beginning of this pregnancy..."

On 'Compazine', 5 mg. q.i.d., this severe case of nausea and vomiting of pregnancy showed "almost immediate response." She had no nausea or vomiting after starting 'Compazine' therapy.



*Compazine**

for prompt control of nausea and vomiting of pregnancy

Available: Tablets, Ampuls and Spansule® sustained release capsules.

Smith, Kline & French Laboratories, Philadelphia

*T.M. Reg. U.S. Pat. Off. for prochlorperazine, S.K.F.

Presenting... an advance in

the treatment of **VAGINITIS**

TRICO

VAGINAL SUPPOSITORIES AND POWDER

a new specific moniliacide

MICOFUR[T. M.]

BRAND OF NIFUROXIME

now added to the established specific trichomonacide

FUROXONE®

BRAND OF FURAZOLIDONE

IMPROVED

FUROXONE®

Rapid relief of burning and itching often within 24 hours

85% CLINICAL CURES* In 219 patients with either trichomonal vaginitis, monilial vaginitis, or both, clinical cures were secured in 187.

71% CULTURAL CURES* 157 patients showed negative culture tests at 3 months follow-up examinations.

Eliminates malodor

Esthetically acceptable, non-irritating

Simple two-step treatment swiftly brings relief and control of vaginal moniliasis and trichomoniasis.

STEP 1 *Office* administration of TRICOFURON VAGINAL POWDER [redacted] [Micofur 0.5% (*anti* 5-nitro-2-furaldoxime), the new nitrofuran fungicide, and Furoxone 0.1% in an acidic water-soluble powder base]. Applied by the physician at least once a week, except during menstruation.

For easy insufflation: plastic insufflator of 15 Gm., supplied with 3 sanitary disposable tips. Also available: glass bottle of 30 Gm.

STEP 2 Continued *home* use to maintain moniliacidal-trichomonacidal action: TRICOFURON VAGINAL SUPPOSITORIES [redacted] (Micofur 0.375% and Furoxone 0.25% in a water-miscible base). Employed by the patient each morning and night the first week and each night thereafter—through one cycle, especially during the important menstrual days.

Box of 12, each hermetically sealed in green foil.

*Combined results of 12 clinical investigators. Data available on request.

NITROFURANS ...a *new* class of antimicrobials ...
neither antibiotics nor sulfonamides

EATON LABORATORIES, NORWICH, NEW YORK

Easier Childbirth

The
National
Drug
Company
is proud to announce
a significant
advance
in the relief
of pain
and the
shortening of labor
in childbirth.

Cervilaxin

NATIONAL brand of relaxin

for shorter labor,
...easier delivery

Answers to some questions on Cervilaxin[1,2]

Q. What is Cervilaxin?

A. Cervilaxin is a new, highly purified form of relaxin, a hormone normally produced at term.

Q. When is it indicated?

A. Cervilaxin is of value in frank labor with slow cervical dilatation, and, with oxytocin, for induction of labor and uterine dysfunction.

Q. What are its advantages?

A. Cervilaxin eases and shortens labor (see Fig. 1): less pain, less trauma, less need for intervention. It lessens danger of fetal damage (brain injury).

Cervilaxin makes oxytocin safer since there is less likelihood of uterine rupture or other adverse effects.

Q. How does it act?

A. Cervilaxin softens the cervix so that it offers less resistance to passage of the fetus; dilatation is facilitated.

Q. Is Cervilaxin recommended for controlling premature labor?

A. No. In massive doses Cervilaxin may retard uterine contractions and prevent premature birth, but this effect is not evident in the smaller doses recommended here.

Q. Is Cervilaxin indicated only in primiparas?

A. No, Cervilaxin has been used with good results in primiparas, and in multiparas with a history of previous difficult labor.

Q. Does Cervilaxin interfere with necessary uterine contractions during labor?

A. No. In recommended dosage there is no interference with well established, regular and normal physiological functions before, during, or after delivery.

Q. What effect does Cervilaxin have on other drugs given during delivery?

A. Cervilaxin does not interfere with the action of any of the drugs commonly employed before, during, or after delivery.

Q. What side effects have been observed?

A. To date, none.

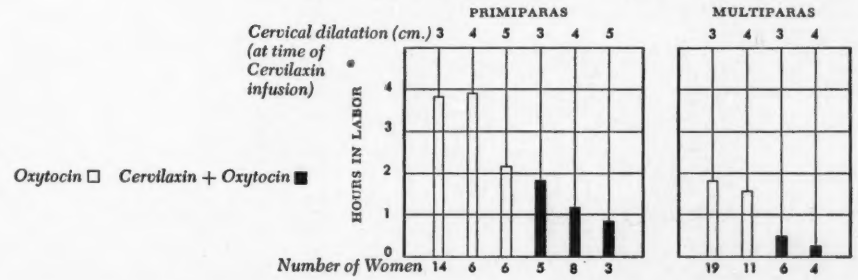
Q. How is Cervilaxin administered?

A. By intravenous drip.

Q. What is the dose?

A. Cervilaxin is supplied in 2 ml. vials containing 20 mg./ml. Usually this one dose is sufficient. Complete dosage and administration instructions are in the package literature.

Fig. 1. Time in labor—Oxytocin vs. Cervilaxin plus Oxytocin



1. Adapted from Birnberg, C. H. and Abitbol, M. M.: Refined Relaxin and Length of Labor, Obst. & Gynec., in press.
2. Eisenberg, L.: Facilitation of Full-Term Labor with Relaxin, in press.

Products of Original Research

NATIONAL

THE NATIONAL DRUG COMPANY
Philadelphia 44, Pa.

CE-903/57

New!

IMPORTANT THERAPY

with

Specific Topical Benefits

in

Pruritus Vulvae Et Ani
Kraurosis Vulvae
Postmenopausal Vaginitis

Hist-A-Cort-E™ pH 4.7

Creme

INCORPORATED IN EXCLUSIVE ACID MANTLE® VEHICLE

ACID MANTLE® Hydrocortisone-Estrone-Pyrilamine Maleate-Synthetic Vitamin A

providing

Epithelium Regenerative
Antiinflammatory
Antipruritic
Antikeratotic
Antiallergic
Antihistaminic
Normal-Vaginal- and Anal-Tract- pH-Restorative

action

Sig. Apply twice daily—Supply 1 oz. tubes

DOME *Chemicals Inc.*

109 WEST 64 ST., NEW YORK 23, N.Y. In Canada: 2765 Bates Rd., Montreal, P.Q.

What is a Sensible Breakfast?

IN PRENATAL NUTRITION
In the aim for optimal nutrition without undue weight gain during the entire prenatal period, oatmeal serves well as a universally accepted food high in nutrient value without "empty" calories.

Since a high percentage of gravid women forego or skimp breakfast, the physician might well point out the need for a sensible breakfast: a meal which provides energy for a morning of productive work, which allays hunger until the noon meal, which supplies an adequate share of the day's nutrient requirements, and which consists of inviting, easily digested foods.

A dish of oatmeal helps fulfill the requirements of such a breakfast: It provides readily available energy; it helps to allay hunger throughout the morning; it makes a notable contribution to the day's nutritional needs; it fits into virtually every breakfast, including most of those especially low in calories.*

Oatmeal is richer in protein than other whole-grain breakfast cereals. None are as high in thiamine as oatmeal. Also, oatmeal provides other B-complex vitamins. Its mineral content, especially of iron and phosphorus, rates it among the leaders.

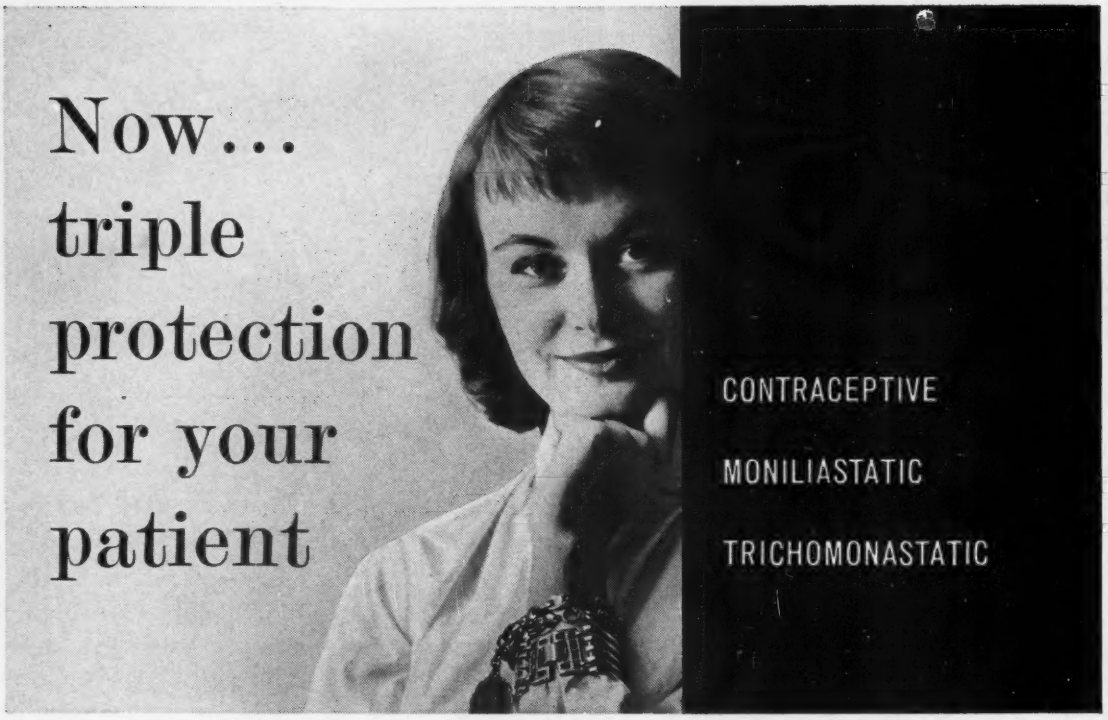
Its delicious taste and easy digestibility further qualify oatmeal as an ideal "habit food" for a sensible breakfast.

Quaker Oats and Mother's Oats, the two brands of oatmeal offered by The Quaker Oats Company, are identical. Both brands are available in the Quick (cooks in one minute) and the Old-Fashioned varieties which are of equal nutrient value.

***WHEN THE DAY'S CALORIE ALLOWANCE IS**

1400 CALORIES OR LESS PER DAY	2400 CALORIES PER DAY	3000 CALORIES OR MORE PER DAY
Breakfast	**Breakfast**	**Breakfast**
Approximately 300 Calories	**Approximately 500 Calories**	**Approximately 700 Calories**
Orange juice, 4 oz.	Orange juice, 4 oz.	Orange juice, 4 oz.
Oatmeal, 1 oz. Skim milk, 4 oz. Sugar, 1 tsp.	Oatmeal, 1 oz. Milk, 4 oz. Sugar, 1 tsp.	Oatmeal, 1 oz. Milk, 4 oz. Sugar, 1 tsp.
Toast, 1 slice lightly buttered	One egg	Two eggs
†Coffee without cream or sugar	Toast, 2 slices with butter or jelly	Bacon, 2 strips
	†Coffee with cream and sugar	Toast, 2 slices with butter or jelly
†For children substitute 4 oz. skim milk		†Coffee with cream and sugar

The Quaker Oats Company
CHICAGO



LANTEEN® JELLY

The preferred LANTEEN diaphragm and jelly technique of contraception affords extra benefits to patients susceptible to trichomonas reinfestation and moniliasis. LANTEEN jelly is not only spermicidal, but also trichomonastatic and moniliastatic. No need to change to condom method. No extra cost.

LANTEEN contraceptive jelly enables all your patients to use continuously the safest conception control method. Even your problem patients do not have to interrupt the diaphragm-jelly technique. The evident increase in the incidence of moniliasis suggests the use of a contraceptive that has been shown in the laboratory to be moniliastatic. Also, LANTEEN jelly's proven activity against trichomonas can aid in preventing reinfection with this organism by the male partner.

Write for complete details of LANTEEN's triple protection.

NOTE: LANTEEN JELLY IS NOT A TREATMENT FOR CLINICALLY ACTIVE MONILIASIS OR TRICHOMONIASIS

LANTEEN JELLY CONTAINS RICINOLEIC ACID 0.50%, HEXYLRESORCINOL 0.10%, CHLOROTHYMOL 0.0077%, SODIUM BENZOATE AND GLYCERIN IN A TRAGACANTH BASE. DISTRIBUTED BY GEORGE A. BREON & COMPANY, 1450 BROADWAY, NEW YORK 18, N. Y. (IN CANADA: E. & A. MARTIN RESEARCH LTD., 20 RIPLEY AVE., TORONTO, CANADA) MANUFACTURED BY ESTA MEDICAL LABORATORIES, INC., CHICAGO 38, ILLINOIS.

Prescribe LANTEEN JELLY *for comprehensive conception control.*

during labor...

during delivery...

following delivery...

"THORAZINE* reduces the tendency to vomit . . . **and gives the patient almost a detached attitude toward her hospital environment and to labor."** –Bonello, F.J.: Internat. Rec. Med. & Gen. Pract. Clin. *169*:197 (April) 1956.

Based on his use of 'Thorazine' during active labor in 110 cases, Bonello finds a double benefit in its administration:

1. Reduced anxiety and apprehension. "The patient becomes placid in her outlook . . . continues to have labor pains regularly, but is almost somnolent between pains . . ."
2. Less danger of aspiration. By substantially reducing the incidence of vomiting, 'Thorazine' improves the patient's safety during anesthesia. No cases of postpartum pneumonia due to aspiration were noted.

Available: Ampuls, Tablets, Syrup (as the hydrochloride), and Suppositories (as the base).

Smith, Kline & French Laboratories, Philadelphia

*T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.

Gynec.

MANUFACTURING PHARMACISTS TO THE MEDICAL PROFESSION SINCE 1870

LLOYD BROTHERS, INC.

CINCINNATI 3, OHIO

October 1, 1957

SUBJECT: Erythropoietin and Cobalt

Dear Doctor:

Among the most intriguing of body processes has been the mechanism which regulates erythropoiesis and iron metabolism. Recent studies have connected these two subjects and have related the action of cobalt to both.

New Hormone Erythropoietin

The work of many investigators has now culminated in the discovery of Erythropoietin (the erythropoietic hormone).[1,2,3,4] They have confirmed that the newly discovered hormone controls the rate of red blood cell production, and that the rate of R B C formation controls the rate of absorption[5] and utilization of iron.

Cobalt Erythropoietin Relationship

Finally, it has been discovered that, acting through physiologic channels, therapeutic cobalt . . . increases red cell production by enhancing the formation of erythropoietin.[6] This provides for the first time the key to the treatment of anemia.

Clinical Superiority

In the common anemias, cobalt-induced erythropoietin provides increases in R B C production resulting in a maximum increase in the absorption and utilization of iron. This explains the superior

clinical results obtained with the administration of therapeutic cobalt and iron.

In Anemia - Less Iron Required →

Roncovite MF is the new therapeutic agent based on erythropoietin formation which translates these new discoveries into the practical utility of full iron effectiveness with greatly decreased, better tolerated iron dosage.

Cordially yours,
LLOYD BROTHERS, INC.

Robert H. Woodward
President

RHW/JP

References

1. Linman, J. W., and Bethell, F. H.: Blood 11:310, 1956. 2. a) Erslev, A. J.: Humoral regulation of red cell production. Blood 8:349, 1953. b) Erslev, A. J., and Lavietes, P. H.: Observation on the nature of the erythropoietic serum factor. Blood 9:1055, 1954. 3. a) Gordon, A. S.; Piliero, S. J.; Kleinberg, W., and Freedman, H. H.: A plasma extract with erythropoietic activity. Proc. Soc. Exper. Biol. & Med. 86:255, 1954. b) Gordon, A.; Piliero, S.; Tanenbaum, M., and Siegel, C.: Erythropoietic action of a plasma filtrate in hypophysectomized rats. Proc. Soc. Exper. Biol. & Med. 89:246, 1955. 4. a) Fried, W.; Plzak, L. F.; Jacobson, L. O., and Goldwasser, E.: Proc. Soc. Exper. Biol. & Med. 92:203, 1956. b) Plzak, L., et al.: J. Lab. Clin. Med. 46:671, 1955. 5. Bothwell, T. H.; Pribella, W. V., and Hurtado, A.: Intro. by C. A. Finch, 6th Congress, Int. Soc. of Hematology, Boston, Sept. 1, 1956. 6. Goldwasser, E.; Jacobson, L. O.; Fried, W., and Plzak, L.: Science 125:1085 (May 31) 1957.

NEW RONCOVITE MF
(MODIFIED FORMULA)

ENHANCES ERYTHROPOIETIN FORMATION

TO RAPIDLY CORRECT ANEMIA WITH LOW IRON DOSAGE.

Each green enteric-coated tablet contains:
Cobalt chloride (Cobalt as Co 3.7 mg.) ..... 15 mg.
Ferrous sulphate, exsiccated ..... 100 mg.

LLOYD BROTHERS, INC. | CINCINNATI 3, OHIO

in urinary tract infections during pregnancy and the puerperium

FURADANTIN®

BRAND OF NITROFURANTOIN

"FURADANTIN possesses such desirable characteristics as stability, a wide antibacterial spectrum, and little tendency to permit development of bacterial resistance; considerations which are particularly important when treating the pregnant patient."[1]

A recent report by Nesbitt and Young[1] emphasizes the unique value of FURADANTIN *in the treatment of urinary tract infections associated with pregnancy. The following highlights from this paper impressively document* FURADANTIN'S *effectiveness and safety:*

THE CLINICAL SAMPLE: "A total of 104 women with bacterial infections of the urinary tract were treated with FURADANTIN during pregnancy and the puerperium . . . The clinical diagnoses included chronic or recurrent cystitis and pyelonephritis."

CLINICAL AND BACTERIOLOGIC RESULTS: "FURADANTIN was highly effective in the treatment of these infections during all stages of pregnancy and the postpartum period. . . . Of the 42 patients treated with 100 mg. FURADANTIN q.i.d., 27 (69 per cent) were cured bacteriologically and clinically; the remaining 15 became asymptomatic but continued to harbor the pathogens as shown by culture. There were no clinical failures in this group. In most patients the beneficial effect of treatment was obvious within the few few days."

SIDE EFFECTS: "Side effects of FURADANTIN therapy were noted in only 17 patients and were mostly quite mild and inconsequential. . . . The obstetric course was satisfactory in all, and there was no evidence that the fetus was in any way affected by the therapy."

CONCLUSIONS: "FURADANTIN, in doses up to 100 mg. q.i.d. for a period of 7 days, is an effective and safe antibacterial chemotherapeutic agent for urinary tract infections. Pregnancy does not contraindicate its use."

FURADANTIN *effective and safe in pregnancy* [1,2,3]

AVERAGE FURADANTIN DOSAGE IN PREGNANCY: Acute complicated, refractory or chronic urinary tract infections—100 mg. q.i.d. Acute uncomplicated urinary tract infections—50 mg. q.i.d. (If patient unresponsive after 2 or 3 days, increase dose to 100 mg. q.i.d.)

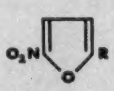
ADMINISTRATION: With meals and with food or milk on retiring. Continue for 3 days after urine becomes sterile.

SUPPLIED: Tablets, 50 and 100 mg., bottles of 25 and 100.
Oral Suspension, 25 mg. per 5 cc. tsp., bottle of 60 cc.
(Readily miscible with water, milk or fruit juices.)

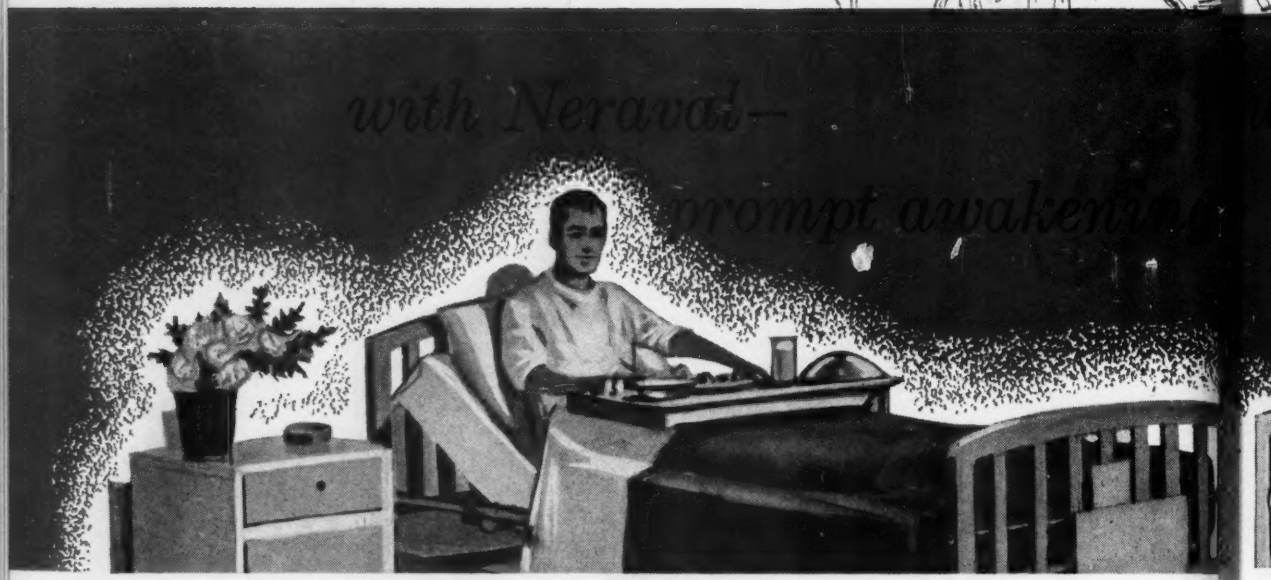
REFERENCES: 1. Nesbitt, R. E. L., Jr., and Young, J. E.: Obst. Gyn., N. Y. 10:89, 1957. 2. Diggs, E. S.; Prevost, E. C., and Valderas, J. G.: Am. J. Obst. 71:399, 1956. 3. MacLeod, P. F.; Rogers, G. S., and Anzlowar, B. R.: Internat. Rec. Med. 169:561, 1956.

NOW, for hospitalized patients, for severe urinary tract infections when peroral administration of FURADANTIN is not feasible and for serious infections as septicemia (bacteremia) when the bacterium is sensitive:
NEW, LIFESAVING FURADANTIN *Intravenous Solution*

NITROFURANS . . . a *new* class of antimicrobials . . .
neither antibiotics nor sulfonamides



EATON LABORATORIES, NORWICH, NEW YORK



A PRACTICAL ADVANCE

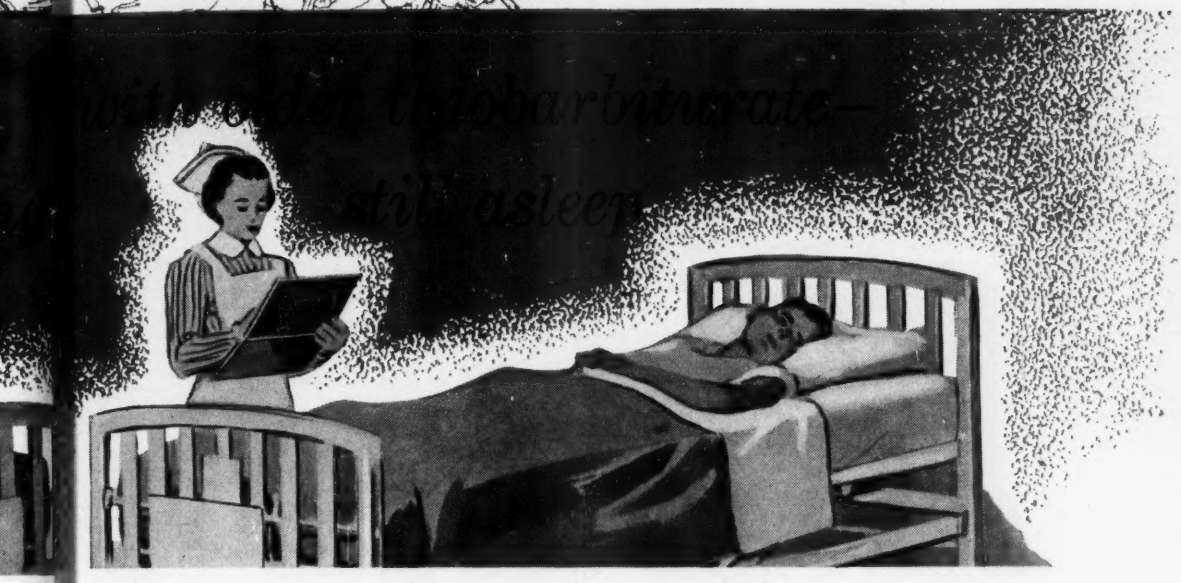
Neraval
SODIUM

in thiobarbiturate anesthesia

- *for oral surgery and related E.N.T. procedures*
- *outpatient clinic surgery* • *office instrumentation and biop*
- *psychiatric electronarcosis and other treatments*
- *orthopedic and fracture procedures in the clinic*

and many other situations in which advantageous use can be made of "...the shortest-acting thiobarbiturate so far.

Schering



...distinctive among thiobarbiturates for its briefer action and lesser tendency to accumulation

NERAVAL is detoxified and eliminated faster than thiopental or thiamylal.[1-5] With NERAVAL, therefore, there is prompt, lucid awakening and a more rapid, notably more complete recovery than with other intravenous anesthetics.[1,3,5-8]

This characteristically swift NERAVAL recovery renders thiobarbiturate anesthesia pleasant for the patient and practical for the physician. For the patient—less postoperative "hangover" depression and incapacity; for the physician—less need of postanesthetic supervision and attention.[1,6-8] Use of NERAVAL simplifies the procedure and makes it more widely convenient for medical practice.

Since NERAVAL has lower milligram potency than earlier thiobarbiturates, it permits very quick lightening of anesthesia and requires higher dosage for equivalent anesthetic effect.

Packaging:
NERAVAL Sodium Sterile Powder:
vials of 1 Gm. and 2 Gm., boxes of 6 and 25;
vial of 5 Gm., boxes of 1 and 25.

Bibliography:
(1) Boone, J. D.; Muñoz, R., and Dillon, J. B.: Anesthesiology *17*:284, 1956. (2) Zima, O.; von Werder, F. and Hotovy, R.: Anaesthesist *5*:244, 1954. (3) Mersch, M. A.; Clarie, D'A., and Fitzpatrick, L. J.: J.M. Soc. New Jersey *53*:414, 1956. (4) Blake, M. W., and Perlman, P. L.: J. Pharmacol. & Exper. Therap. *117*:287, 1956. (5) Irwin, S.; Stagg, R. D., Dunbar, E., and Govier, W. M.: J. Pharmacol. & Exper. Therap. *116*:317, 1956. (6) Ayd, F. J., Jr.: Neraval: A new anesthetic for electroconvulsive therapy, Paper presented at annual meet., Electroshock Research Association, Chicago, Illinois, April 29, 1956. (7) Reifferscheid, M., and Dietmann, K.: Deutsche med. Wchnschr *79*:638, 1954. (8) Houde, J., Hudon, F., and Jacques, A.: Neraval (methitural sodium), Paper presented at Meet., Canad. Anaesth. Soc., Quebec City, P. Q., May 5, 1956.

NERAVAL® Sodium, brand of methitural sodium.

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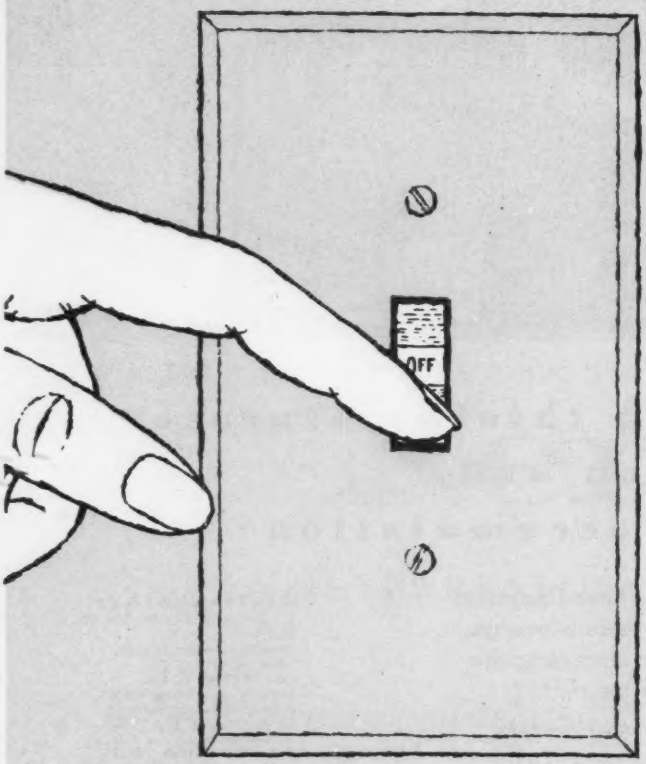

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REFERENCES

(1) Chan, Y. T. and Hays, E. E., The American Journal of the Medical Sciences, August 1957; (2) Townsend, E. H., Jr., In Press; (3) Weismiller, F., In Press; (4) Cass, Leo J. and Frederik, W. S., In Press.

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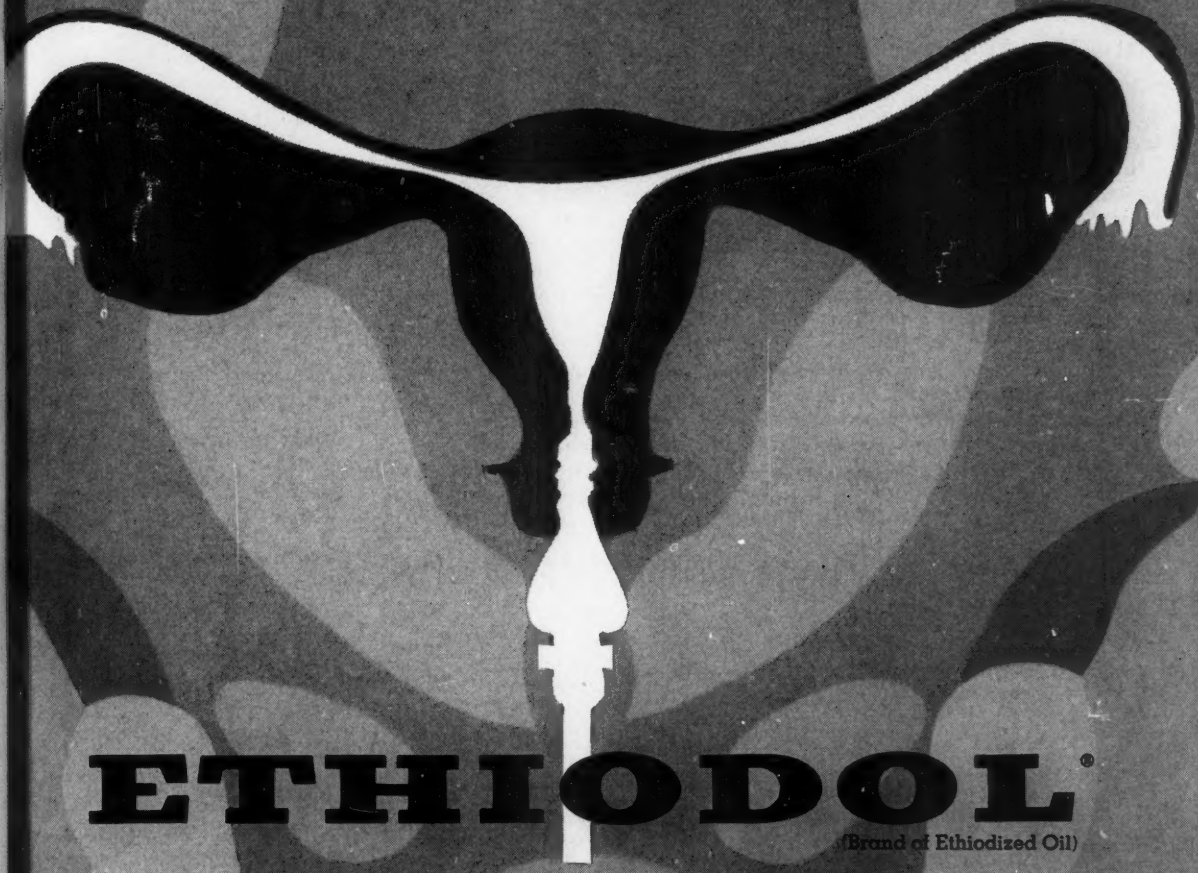

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ENOVID*

BRAND OF NORETHYNODREL WITH ETHYNYLESTRADIOL 3-METHYL ETHER

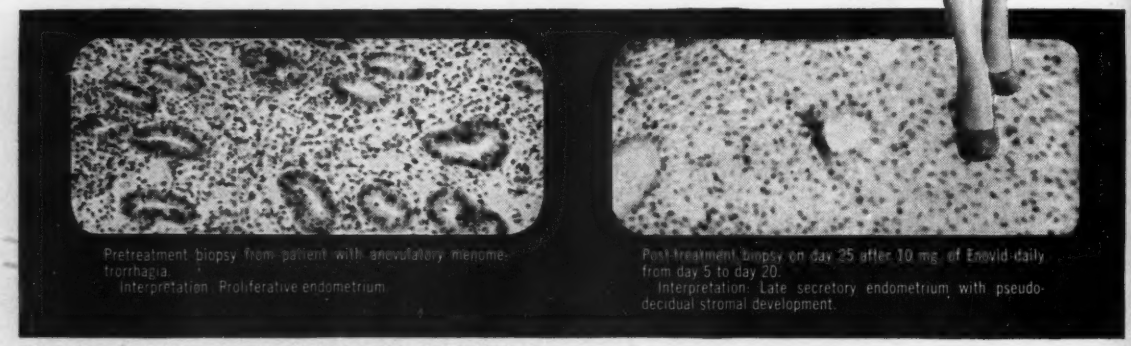
Regulates menstrual disorders through reliable endometropic control

Enovid is Searle's new, orally effective agent designed to provide specific control of menstrual disorders.

Enovid contains norethynodrel, a new synthetic steroid with strong progestational and lesser estrogenic activity. The estrogenic effect, enhanced by the addition of ethynylestradiol 3-methyl ether, prevents spotting or breakthrough bleeding in most patients in whom it would otherwise occur.

Like the normal endocrine action of the corpus luteum, Enovid maintains the integrity of the endometrium during administration of the drug. Moreover, as occurs on withdrawal of the natural hormone, the withdrawal of Enovid results in the flow characteristic of menstruation. Also, as does the natural hormone, Enovid controls the gonadotropic functions of the anterior pituitary glands.

This specific control of the menstrual cycle permits effective treatment of both excessive and inadequate endometrial activity and provides the physician with a dependable agent for treating such disorders as amenorrhea, dysmenorrhea, menorrhagia, metrorrhagia and premenstrual tension.



Pretreatment biopsy from patient with anovulatory menometrorrhagia.
Interpretation: Proliferative endometrium.

Post-treatment biopsy on day 25 after 10 mg. of Enovid daily from day 5 to day 20.
Interpretation: Late secretory endometrium with pseudodecidual stromal development.

Biopsy photomicrographs courtesy of Anna L. Southam, M.D., New York, N.Y.

INDICATIONS AND DOSAGE GUIDE FOR ENOVID

DISORDER	FIRST CYCLE	SECOND AND THIRD CONSECUTIVE CYCLES
Menorrhagia	One or two 10-mg. tablets daily to day 25 of the cycle.	One 10-mg. tablet daily from day 5 to day 25*
Metrorrhagia	One or two 10-mg. tablets daily to day 25 (or for 10 days to establish cycle)	same as above
Amenorrhea (primary or secondary)	One 10-mg. tablet daily for 20 days to establish cycle	same as above
Oligomenorrhea	One 10-mg. tablet daily from day 5 to day 25*	same as above
Premenstrual Tension	One 10-mg. tablet daily from day 5 to day 25*	same as above
Dysmenorrhea	One 10-mg. tablet daily from day 5 to day 25	One 10-mg. tablet daily from day 5 to day 25
Inadequate Luteal Phase	One 10-mg. tablet daily from day 15 to day 25	One 10-mg. tablet daily from day 15 to day 25

*The administration of Enovid prior to day 15 may interfere with ovulation; if anovulatory cycles are not desired, one 10-mg. tablet of Enovid should be administered daily from day 15 to day 25.

SPECIAL NOTES: (1) If nausea is encountered, the daily dose may be cut in half or given in divided doses for three days and then return to regular dose. (2) Intermenstrual spotting is usually evidence of inadequate dosage. This type of bleeding is usually controlled by increasing the dosage one 10-mg. tablet daily. (3) Following discontinuance of treatment, the intermenstrual interval of the first untreated cycle is commonly prolonged for approximately one week.

FORMULA: Each 10-mg. tablet of Enovid (available as uncoated, scored, coral tablets) contains norethynodrel, a new synthetic steroid, with 0.15 mg. of ethynylestradiol 3-methyl ether.

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PRENATAL CAPSULES LEDERLE

for an active pregnancy

NEW better tolerated source of iron—ferrous fumarate—helps eliminate gastric upset. **NEW** non-inhibitory intrinsic factor assures greater B_{12} absorption to meet increased requirements. **NEW** more comprehensive formulation includes *phosphorus-free* calcium, Vitamins K and B_6, plus important minerals and trace elements. **NEW** Reminder Jar . . . she'll keep it handy on the dining table . . . use it later for diaper pins or cotton. *Your patients pay no more for the added benefits of Filibon.*

Each capsule contains:

Vitamin A	4,000 U.S.P. Units
Vitamin D	400 U.S.P. Units
Thiamine Mononitrate (B_1)	3 mg.
Pyridoxine (B_6)	1 mg.
Niacinamide	10 mg.
Riboflavin (B_2)	2 mg.
Vitamin B_{12}	2 mcgm.
Ascorbic Acid (C)	50 mg.
Vitamin K (Menadione)	0.5 mg.
Folic Acid	1 mg.
Ferrous Fumarate	90 mg.
Iron (as Fumarate)	30 mg.
Intrinsic Factor	5 mg.
Fluorine (as CaF_2)	0.015 mg.
Copper (as CuO)	0.15 mg.
Iodine (as KI)	0.01 mg.
Potassium (as K_2SO_4)	0.835 mg.
Manganese (as MnO_2)	0.05 mg.
Magnesium (as MgO)	0.15 mg.
Molybdenum (as $Na_2MoO_4 \cdot 2H_2O$)	0.025 mg.
Zinc (as ZnO)	0.085 mg.
Calcium Carbonate	575 mg.

Dosage: One or more capsules daily.
Supplied: Attractive, re-usable bottles of 100 capsules.

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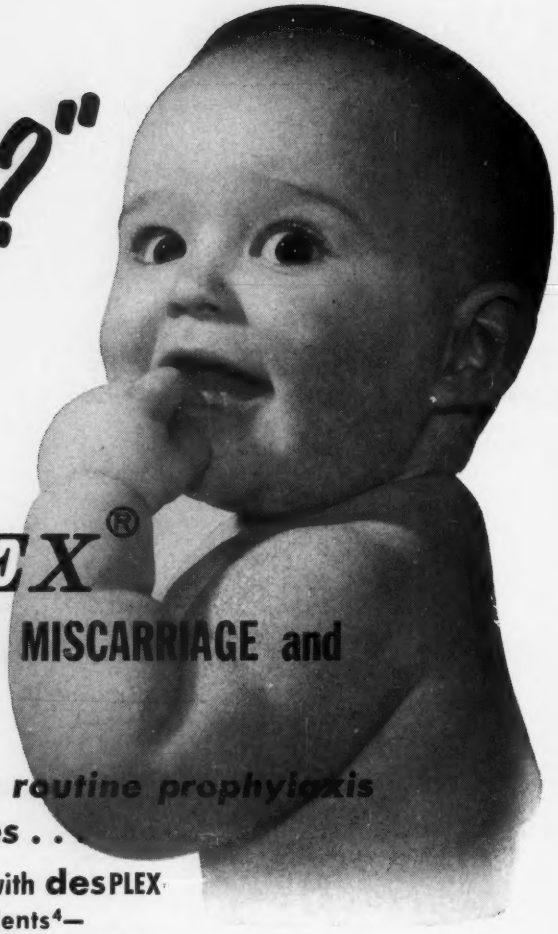
"Really?"



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(Each **des**PLEX tablet starts with 25 mg. of diethylstilbestrol, U.S.P., which is then ultramicronized to smooth and accelerate absorption and activity. A portion of this ultramicronized diethylstilbestrol is even included in the tablet coating *to assure prompt help in emergencies.* **des**PLEX tablets also contain vitamin C and certain members of the vitamin B complex to aid detoxification in pregnancy and the effectuation of estrogen.)

For further data and a generous trial supply of **des**PLEX, write to:
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REFERENCES

1. Canario, E. M., et al.: Am. J. Obst. & Gynec. 65:1298, 1953.
2. Gitman, L., and Koplowitz, A.: N. Y. St. J. Med. 50:2823, 1950.
3. Karnaky, K. J.: South. M. J. 45:1166, 1952.
4. Peña, E. F.: Med. Times 82:921, 1954; Am. J. Surg. 87:95, 1954.
5. Ross, J. W.: J. Nat. M. A. 43:20, 1951; 45:223, 1953.

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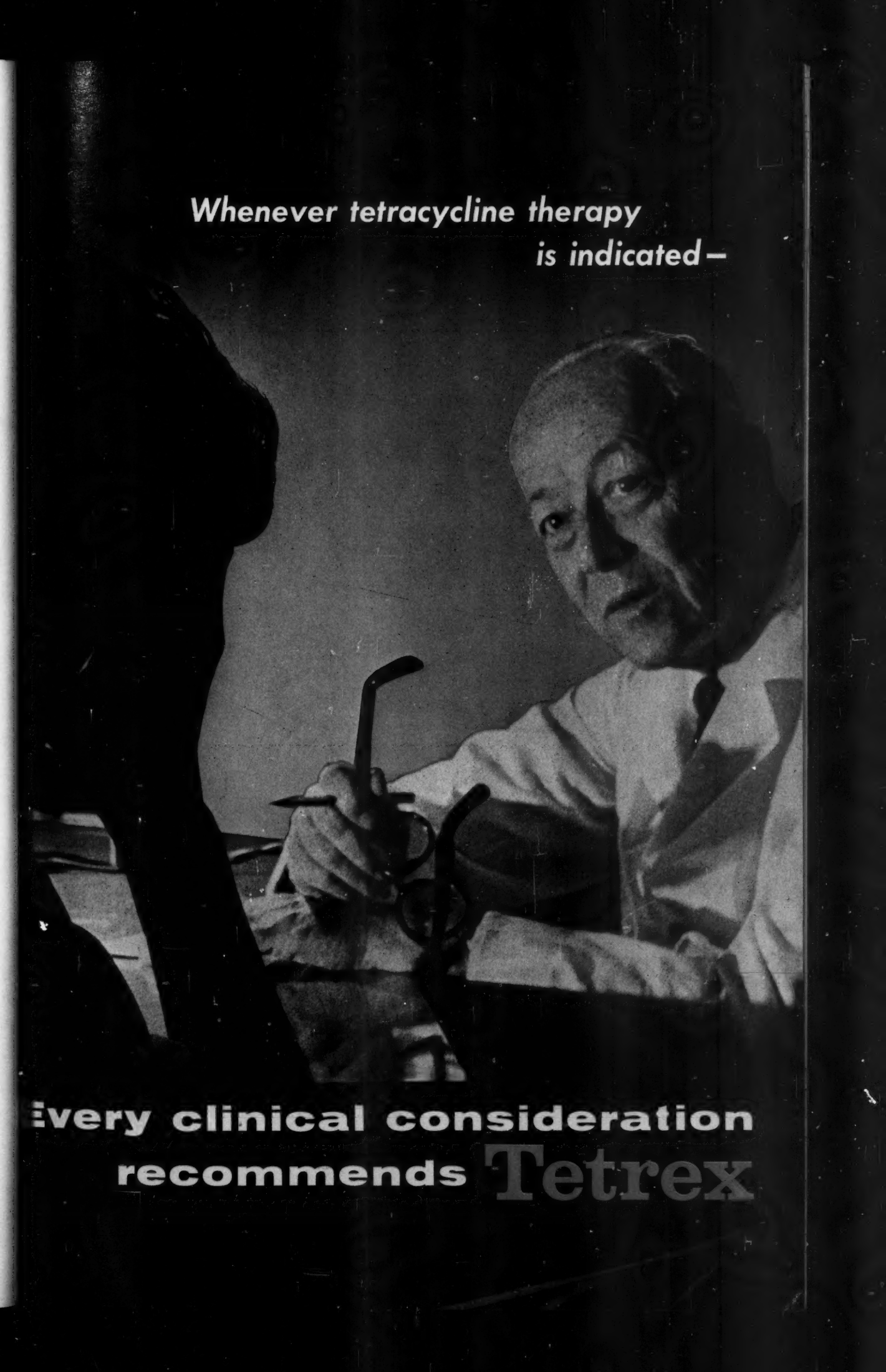
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is indicated—
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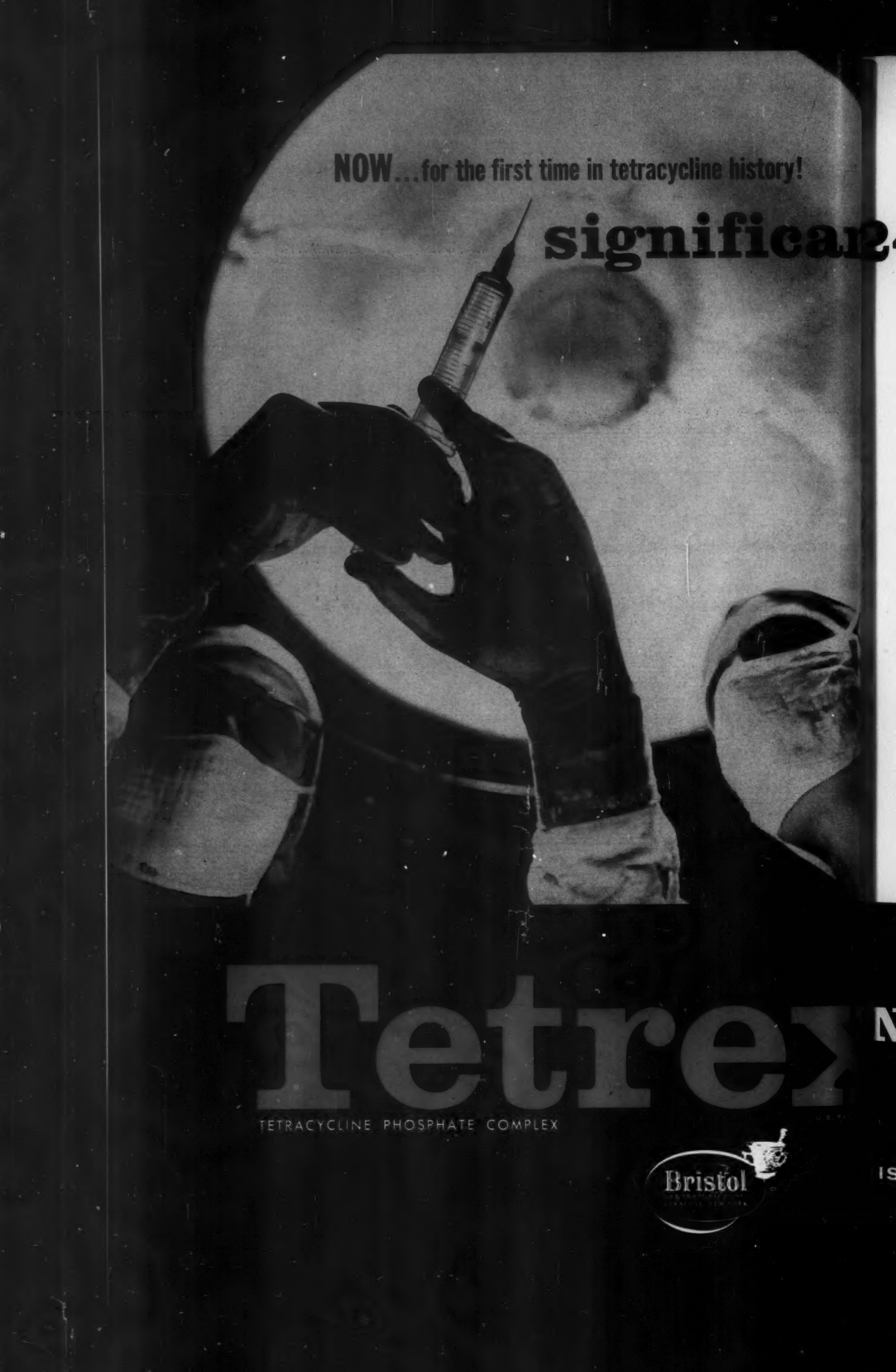
recommends Tetrex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on a **SINGLE** intramuscular dose, in minimal injection volume

This achievement is made possible by the unique solubility of TETREX (tetracycline phosphate complex), which permits *more* antibiotic to be incorporated in *less* volume of diluent. Clinical studies have shown that injections are well tolerated, with no more pain on injection than with previous, less concentrated formulations.

TETREX Intramuscular '250' can be reconstituted for injection by adding 1.6 cc. of sterile distilled water or normal saline, to make a total injection volume of 2.0 cc. When the entire 250 mg. are to be injected, and minimal volume is desired, as little as 1.0 cc. of diluent need be used. (Full instructions for administration and dosage for adults and children, accompany packaged vial.)

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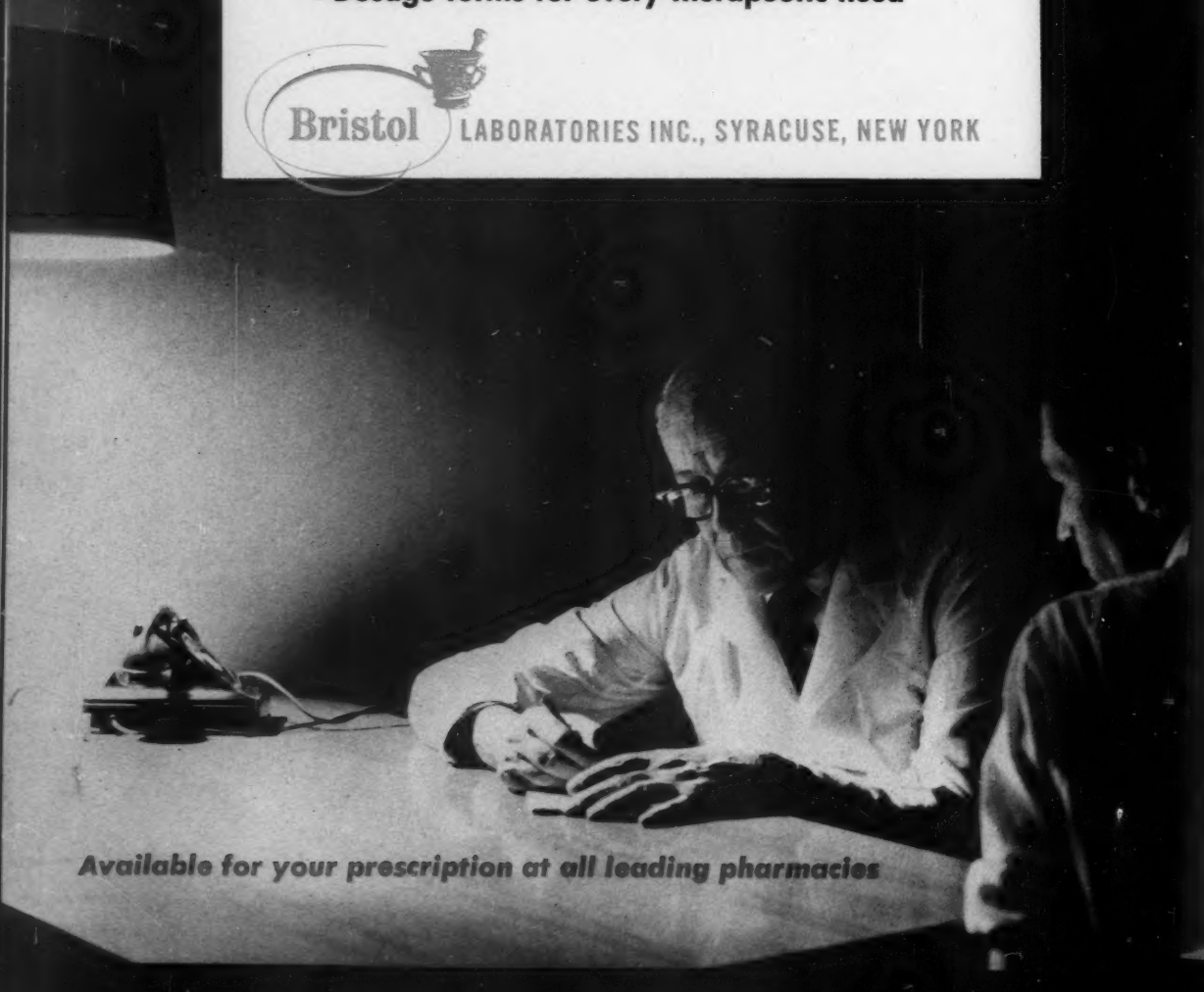

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. . . for months[1-3] of menopausal relief with one 30-day course of therapy. . .

Symptomatic relief is seen promptly[1] after initial therapy begins. Months[1-3] of "striking"[4] menopausal relief results in most cases after a single 30-day course of TACE therapy. Because TACE is uniquely stored in body fat[1]... the menopause is smoother... the important "feeling of well-being"[3,4] is restored... symptoms recur less frequently than with other estrogens.[1-3] There is less withdrawal bleeding with TACE.[1-3] *Dosage: 2 caps. daily for thirty days.*

References: 1. Woodhull, R. B.: Obst. & Gynec. 3:201, 1954. 2. Ausman, D. C.: Wisc. M. J. 53:322, 1954. 3. Edwards, B. E.: J. Indiana M. A. 47:869, 1954. 4. Ivory, H. S.: J. M. Soc. New Jersey 51:273, 1954.

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Bottles of 100, 250 and 1000.

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in postmenopausal vaginitis
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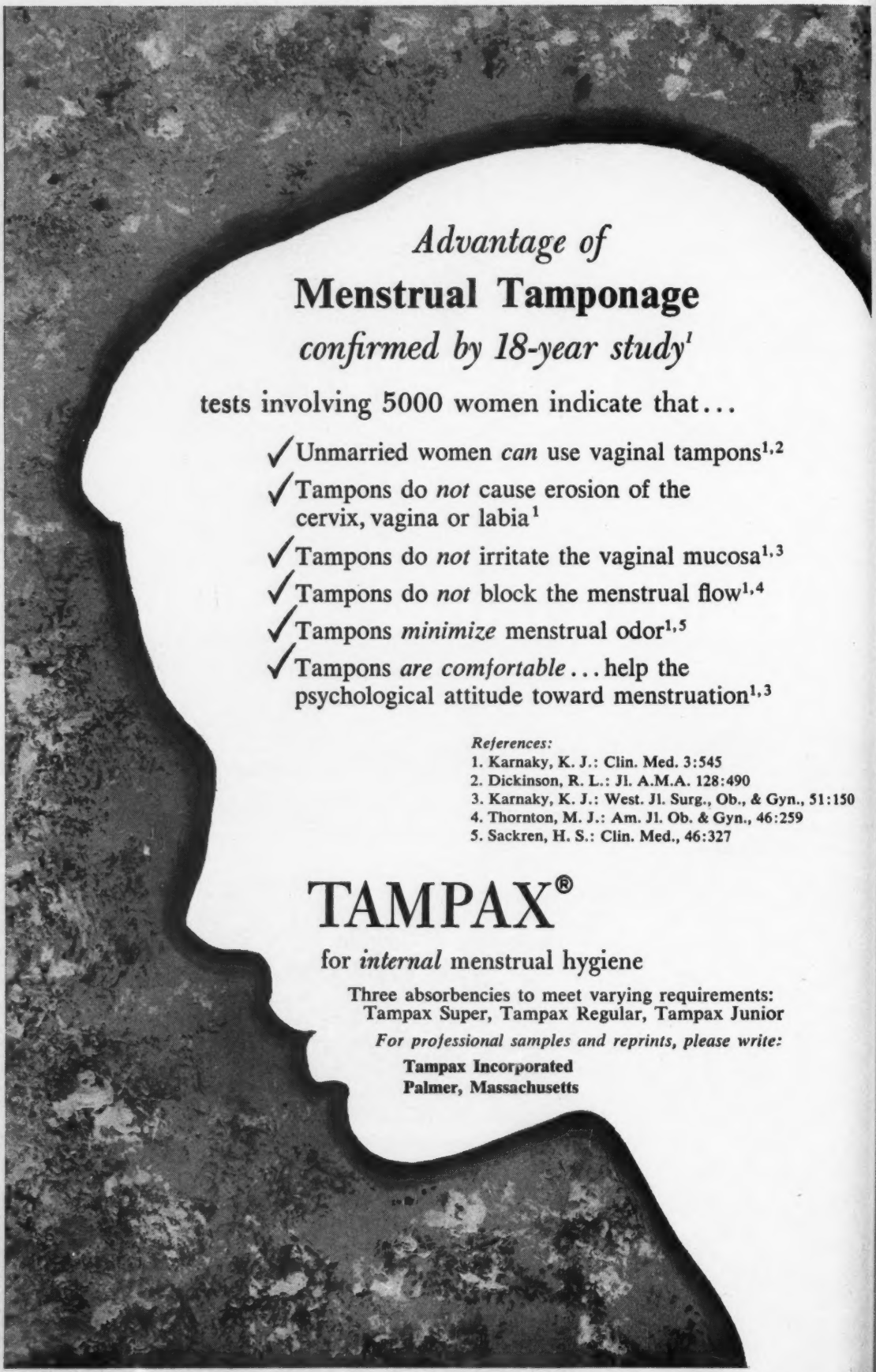

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Menstrual Tamponage

confirmed by 18-year study[1]

tests involving 5000 women indicate that...

- ✓Unmarried women *can* use vaginal tampons[1,2]
- ✓Tampons do *not* cause erosion of the cervix, vagina or labia[1]
- ✓Tampons do *not* irritate the vaginal mucosa[1,3]
- ✓Tampons do *not* block the menstrual flow[1,4]
- ✓Tampons *minimize* menstrual odor[1,5]
- ✓Tampons *are comfortable*... help the psychological attitude toward menstruation[1,3]

References:

1. Karnaky, K. J.: Clin. Med. 3:545
2. Dickinson, R. L.: Jl. A.M.A. 128:490
3. Karnaky, K. J.: West. Jl. Surg., Ob., & Gyn., 51:150
4. Thornton, M. J.: Am. Jl. Ob. & Gyn., 46:259
5. Sackren, H. S.: Clin. Med., 46:327

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for *internal* menstrual hygiene

Three absorbencies to meet varying requirements:
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For professional samples and reprints, please write:

Tampax Incorporated
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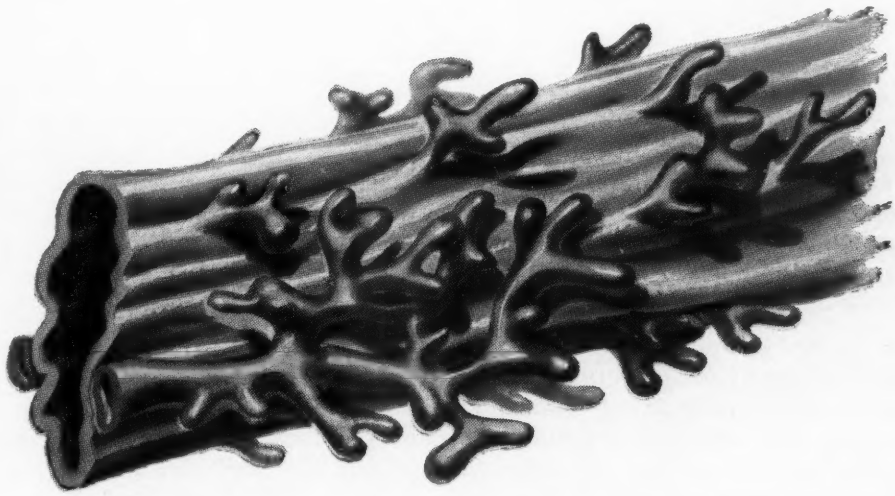
rediscovered:

the female urethra

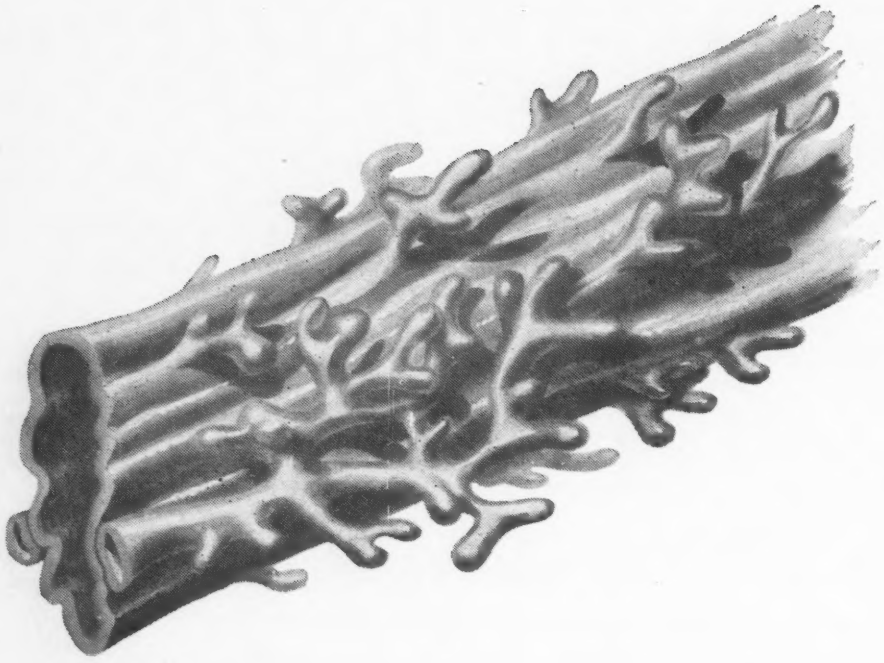
newer knowledge of its structure and cytology provides a clearer understanding of its important role in pelvic distress.



Schematic construction of female urethra demonstrating extensive network of peri-urethral glands, ending in numerous blind pockets. Drainage is into the urethra through small openings along its length, and into the para-urethral (Skene's) ducts.

1. Recent anatomic studies of the female urethra demonstrate a high susceptibility to infection.

A changing concept—The female urethra "was formerly considered only to be a short, simple, straight tube which served solely to empty the bladder. Recent studies have changed our notions concerning this . . . . sections through the urethra and its surrounding tissues have shown numerous glands."[1]



Tortuous, with many interconnections but relatively poor drainage, these glands "form ideal foci for chronic infection."[1] Periurethral gland infection is followed by infiltration and thickening of the urethral wall, hypertrophy and granulation of the urethral mucosa, and constriction of the urethral lumen. The trauma of childbirth and coitus further invites infection of these delicate structures, which are exposed to vaginal and rectal discharges "from the period of diaper life to old age."[1] Thus, the urethra is not only a portal of entry for urologic infection, but the *site* of pathologic change "more frequently than any other portion of the female urinary tract."[2]

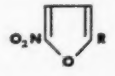
Unrecognized source of pelvic symptoms—Prevalent as it is in women, chronic urethritis "can be easily overlooked" because of the frequency with which the pain and discomfort are referred to other areas.[2] In addition to obvious urinary tract symptoms such as frequency, urgency, pain and burning on urination, chronic urethral infection is often responsible for pain in the lower abdomen and pelvis, lumbosacral region or upper thighs.

BACTERIAL URETHRITIS YIELDS QUICKLY TO

FURACIN® *Urethral Suppositories*

brand of nitrofurazone

Insertion of these suppositories provides gentle dilation; the local anesthetic, diperodon, affords prompt and sustained relief of pain.[3] The antibacterial, FURACIN, achieves wide-spectrum bactericidal action without tissue toxicity. Each suppository contains FURACIN 0.2% and 2% diperodon·HCl in a water-dispersible base. Hermetically sealed in silver foil, box of 12.



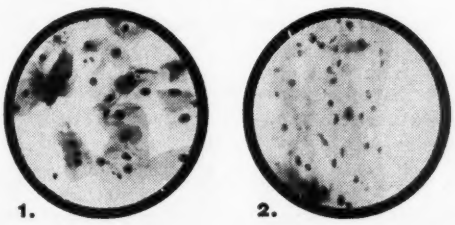
The Nitrofurans—a unique class of antimicrobials . . . Products of Eaton Research

2. Exfoliative cytology explains frequency of dyspareunia and other pelvic complaints in postmenopausal women.

Senile urethritis: often encountered, seldom described—A little known phenomenon has recently been reported by Youngblood and his colleagues.[4,5] Examining smears of epithelial cells from the urethrae of postmenopausal women, they found the same absence of normal, cornified, pyknotic squamous cells as in the vaginal smears, resulting from estrogen deficiency. Leukocytes and even erythrocytes were usually present, as in senile vaginitis. Along with these cytologic alterations, endoscopic examination revealed a hyperemic and atrophic urethral mucosa.

"Senile" urethritis is a common cause of dyspareunia, dysuria and other pelvic discomfort in postmenopausal women. Even when the urethra is recognized as the trouble spot, these women frequently fail to obtain relief because the underlying involutional nature of the urethritis is unsuspected, and antibacterial measures alone are employed. The lesion may resemble closely that of nonspecific urethritis.

"Progressive histologic normalization" parallels rapid symptomatic relief with new Furestrol Suppositories. In their investigations, Youngblood and co-workers[4,5] treated 120 postmenopausal, involutional urethritis patients with FURACIN Urethral Suppositories containing, in addition, 0.1 mg. of diethylstilbestrol. All showed prompt alleviation of symptoms, with disappearance of endoscopic signs of irritation. After 1 to 2 weeks' treatment, the urethral smears returned to normal, indicating replacement of the atrophic mucosa with a healthy, stratified squamous epithelium. These FURACIN-estrogen suppositories are now available as FURESTROL Suppositories.



1. Pretreatment urethral smear of postmenopausal woman with senile urethritis. Basal cells with low nucleocytoplasmic ratio are predominant, with leukocytes and erythrocytes.

2. Urethral smear from same patient after 2 weeks' treatment with FURESTROL Suppositories. The cornified, squamous cells indicate a healthy, normal epithelium.

Ingredients work together—FURACIN eradicated the low grade infection commonly present, while the diethylstilbestrol corrected the atrophic tissue changes. The excellent clinical results achieved with FURESTROL Suppositories could not be approached in control groups treated with suppositories from which any of the ingredients—FURACIN, estrogen, or diperodon, the local anesthetic—had been eliminated.

POSTMENOPAUSAL URETHRITIS YIELDS PROMPTLY TO

NEW FURESTROL T.M. *Suppositories*

Provides estrogen to reverse the involutional changes of senile urethritis, plus the antibacterial, anesthetic and gently dilating action of the FURACIN Urethral Suppository. Each FURESTROL Suppository contains FURACIN 0.2%, diperodon·HCl 2%, and diethylstilbestrol 0.0077% (0.1 mg.), in a water-dispersible base. Hermetically sealed in orchid foil, box of 12.

REFERENCES: 1. Wharton, L. R. in Campbell, M.: Urology, W. B. Saunders Company, Philadelphia and London, 1954, Vol. 2, p. 1390 et seq. 2. Barrett, M. E.: J. M. Ass. Alabama 26:144, 1956. 3. Youngblood, V. H.: J. Urol. 70:926, 1953. 4. Youngblood, V. H.; Tomlin, E. M., and Davis, J. B.: Senile urethritis in women, J. Urol. (in press). 5. Youngblood, V. H.; Tomlin, E. M.; Williams, J. O., and Kimmelstiel, P.: Exfoliative cytology of the senile female urethra, Tr. Southeast. Sect. Am. Urol. Ass. (in press).

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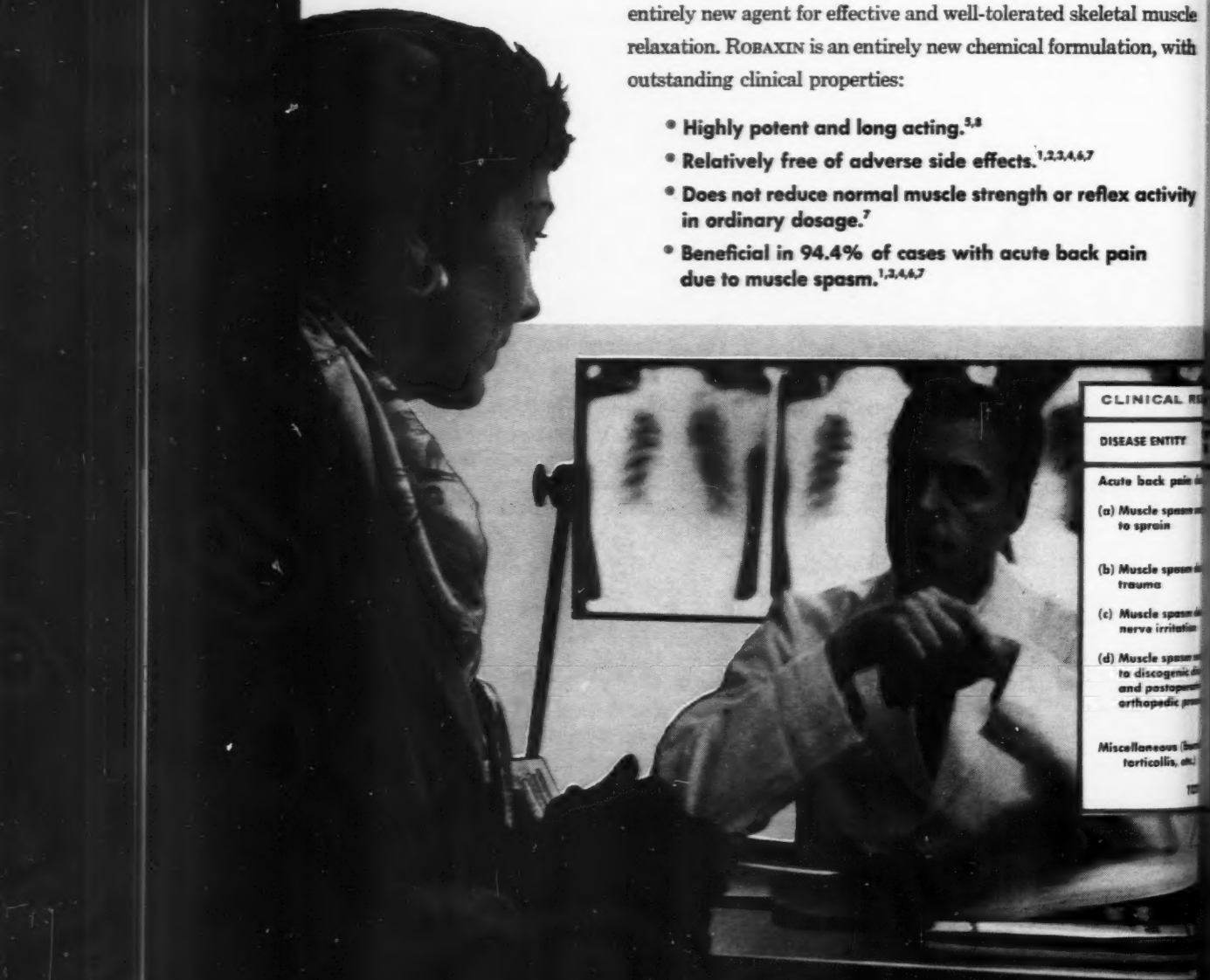
ROBAXIN – synthesized in the Robins Research Laboratories, and intensively studied for five years – introduces to the physician an entirely new agent for effective and well-tolerated skeletal muscle relaxation. ROBAXIN is an entirely new chemical formulation, with outstanding clinical properties:

- **Highly potent and long acting.**[3,8]
- **Relatively free of adverse side effects.**[1,2,3,4,6,7]
- **Does not reduce normal muscle strength or reflex activity in ordinary dosage.**[7]
- **Beneficial in 94.4% of cases with acute back pain due to muscle spasm.**[1,2,4,6,7]



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ROBAXIN is highly specific in its action on the internuncial neurons of the spinal cord – with inherently sustained repression of multisynaptic reflexes, but with no demonstrable effect on monosynaptic reflexes. It thus is useful in the control of skeletal muscle spasm, tremor and other manifestations of hyperactivity, as well as the pain incident to spasm, without impairing strength or normal neuromuscular function.

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ROBAXIN IN ACUTE BACK PAIN[1,3,4,6,7]

DURATION OF TREATMENT	DOSE PER DAY (divided)	RESPONSE marked	mod.	slight	neg.	SIDE EFFECTS
2-42 days	3-6 Gm.	17	1	0	0	None, 16 Dizziness, 1 Slight nausea, 1
1-42 days	2-6 Gm.	8	1	3	1	None, 12 Nervousness, 1
4-240 days	2.25-6 Gm.	4	1	0	0	None, 5
2-28 days	1.5-9 Gm.	24	3	0	3	None, 25 Dizziness, 1 Lightheadedness, 2 Nausea, 2 *
3-60 days	4-8 Gm.	6	0	0	0	None, 6
		59	6	3	4	* Relieved on reduction of dose

References: 1. Carpenter, E. B.: Publication pending. 2. Carter, C. H.: Personal communication. 3. Forsyth, H. F.: Publication pending. 4. Freund, J.: Personal communication. 5. Morgan, A. M., Truitt, E. B., Jr., and Little, J. M.: American Pharm. Assn. 46:374, 1957. 6. Nachman, H. M.: Personal communication. 7. O'Doherty, D.: Publication pending. 8. Truitt, E. B., Jr., and Little, J. M.: J. Pharm. & Exper. Therap. 119:161, 1957.

Indications – Acute back pain associated with: (a) muscle spasm secondary to sprain; (b) muscle spasm due to trauma; (c) muscle spasm due to nerve irritation; (d) muscle spasm secondary to discogenic disease and postoperative orthopedic procedures; and miscellaneous conditions, such as bursitis, fibrositis, torticollis, etc.

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Precautions – There are no specific contraindications to Robaxin and untoward reactions are not to be anticipated. Minor side effects such as lightheadedness, dizziness, nausea may occur rarely in patients with unusual sensitivity to drugs, but disappear on reduction of dosage. When therapy is prolonged routine white blood cell counts should be made since some decrease was noted in 3 patients out of a group of 72 who had received the drug for periods of 30 days or longer.

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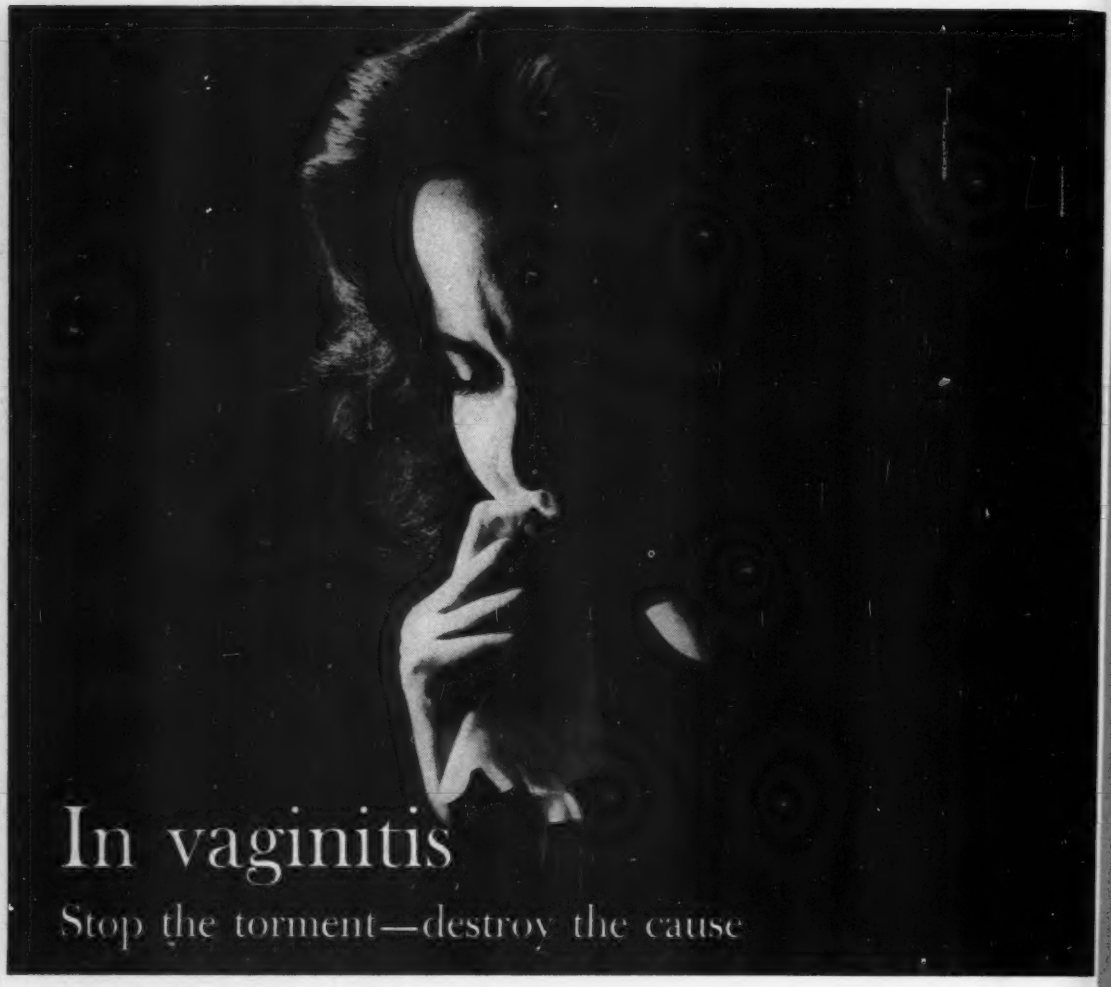

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(1) Cortese, J. T.: Clin. Med. *2*:45, 1955. (2) Hens... H. A.: Postgrad. Med. *8*:293, 1950. (3) Horoschak, A... and Horoschak, S.: J. M. Soc. New Jersey *43*:92, 19...

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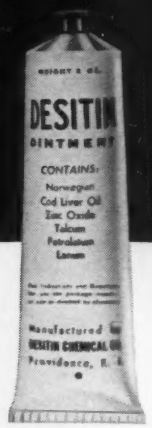

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1. Grayzel, H. G., and Schapiro, S.: Western J. Surg., Obstet. & Gynec., Oct. 1956.

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EVALUATION OF SURGICAL PROCEDURES EMPLOYED FOLLOWING THE FAILURE OF IRRADIATION THERAPY IN CANCER OF THE CERVIX*†

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FROM the profusion of cancer literature today, certain concepts are evolving which represent a modification of heretofore standardized methods of treatment. While this flux of opinion represents a healthy vitality in scientific effort and invariably results in progress, real benefit is obtained only when proper evaluation is made of each innovation or renewed application of previous methods.

One of the principal subjects for scrutiny in contemporary study is the problem of radioresistant lesions. In the past, these cases were afforded only reirradiation or palliative surgery as a gesture at treatment. In the recent decade, the emphasis has shifted to two main considerations, namely, primary eradication by surgery and the cytohistological designation of the resistant

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**Fellow, National Institute of Public Health.
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tumor. In the latter, the potential benefits are tremendous, but this new field of endeavor is in the infancy of its clinical application. To date, the only certain method of determining whether or not a given lesion is radioresistant is to apply a course of radiation therapy and evaluate the case clinically and with repeated cytological smears and biopsies. The cases which present persistent tumor then can be subjected to surgery.

As unsatisfactory and frustrating as this may be, it is the method that must be followed as of today since the treatment of cancer of the cervix is still primarily a radiological one. Table I shows that radiation, even when nonselective, can provide a 5 year survival of 44.4 per cent. The preference for irradiation as primary treatment is widespread[14, 15, 30] and it is unlikely to be displaced by surgery on the basis of present-day statistics. This preference has been further strengthened of late by the growing conviction that when lymph nodes are involved there is very little superiority of one method over another. Beecham[3] is of this opinion, as are Allen, Sherman, and Arneson.[1] These latter authors point out that the same patients are being lost by either method and the answer is either more extensive surgery or better irradiation. This is discouraging to the advocates of surgery whose operation was to prove superior because the lymph nodes were removed.

TABLE I. END RESULTS

	CLINICAL STAGE				TOTAL
	I	II	III	IV	
Primary Cases, 1933-1950.—					
Number admitted	37	82	141	80	340
Survival results	32	53	58	8	151
Percentage	86.5	64.6	41.1	10.0	44.4
Secondary Cases, 1946-1950.—					
Number admitted	5	15	22	46	88
Survival results	2	10	9	3	24
Percentage	40.0	66.6	40.9	6.5	27.2

In the study of any statistical report, the answer to the problem of improved results lies in the "lost" column. It is here that radioresistance is making its influence felt, and it is in the determination of this tumor characteristic that so much effort is being expended. Cytological,[11, 16, 26] cytochemical,[12] and histological[9] methods are being exploited in the attempt to determine radioresistance either prior to or early in therapy. As yet, none of the techniques have been developed to the point where the clinician is willing to base his definitive treatment on the laboratory findings. Since Graham[10] has shown that the radiosensitive lesion does poorly if treated by surgery, a considerable element of doubt plagues any with a tendency to employ surgery as a primary treatment. Meigs[18] has made the statement: "In my opinion . . . the combination of full radiation . . . treatment and radical surgery is a mistake." "Our job is to find out before treatment which is the better method for the individual patient." Novak[20] has pointed out just how difficult this may be prior to clinical extension of the disease.

Proponents of combined therapy[2, 28] feel that preoperative irradiation increases 5 year salvage rates. This contention, however, can be applied only

in a group of selective cases and with the acceptance of a definite increase in risk of fistulas and other surgical complications.

Read[23] has observed that approximately 1.5 per cent of irradiated patients will develop recurrences. This, however, represents only a portion of patients in whom irradiation has failed. The 5 year survival rates in reirradiated patients vary from 2 to 16.4 per cent[6, 27, 29] and, of course, are limited to cases in which a sufficient time interval has elapsed since the original therapy.

There remains, therefore, a place for the evaluation of surgical intervention in cases of irradiation failure, whether this be caused by a primary state of radioresistance or a poorly administered, inadequate course of radiation therapy.

Material

As of December, 1956, 120 operations for pelvic malignancy have been performed on patients who received treatment at the Mercy Hospital Institute of Radiation Therapy. Sixty-nine of these procedures consisted of radical hysterectomy and lymphadenectomy, and 51 involved either complete or partial pelvic exenteration.

TABLE II. RADICAL OPERATIONS

Total Number.—	
Radical hysterectomy	69
Pelvic exenteration (anterior, posterior, total)	51
Total	120
For Radioresistant or Persistent Carcinoma of Cervix.—	
Radical hysterectomy	45
Exenteration (anterior, posterior, total)	35
Total	80

Eighty of these operations were performed for radioresistant or persistent carcinoma of the cervix. Of these 80, 45 were limited to radical extirpation of the uterus and regional lymph nodes, while in 35 all or part of the pelvic viscera were removed in addition to the uterus. The less extensive procedures were distributed according to Table III. Surgery was employed as primary treatment usually when some circumstances indicated the withholding of radiation therapy.

TABLE III. INDICATIONS FOR RADICAL HYSTERECTOMY AND NODE DISSECTION

Recurrent, resistant, or persistent carcinoma (including 3 stump carcinomas)	45	
Primary carcinoma	24	
Teaching cases		14
Stump carcinoma		3
Malignant cervical polyp		1
Refused radiation		3
After Krebiozen therapy		1
Prolapse with carcinoma (Schauta operation)		1
Carcinoma of cervix with benign vesicovaginal fistula		1
Total	69	

The 51 cases of exenteration in Table IV were almost equally distributed among the anterior, posterior, or total classifications, which gave us a fortuitous basis for comparison. Two thirds of these procedures were done for persistent or recurrent disease, and the remainder were for malignancy of other organs. The problems of technique, supportive measures, and postoperative care, however, were essentially the same, and in this regard furnished us additional experience in patient management.

TABLE IV. EXENTERATIONS

Total number of exenterations	51	
Anterior		20
Posterior		17
Total		14
Indications:		
Carcinoma of cervix, recurrent or resistant	35	
Carcinoma of bladder	5	
Carcinoma of rectum	4	
Carcinoma of ovary	2	
Sarcoma of bladder	1	
Carcinoma of endometrium	3	
Carcinoma of urethra	1	
Total	51	

Our incidence of stump cases in this series is 8.1 per cent. This figure like many in recent reports, indicates a mounting frequency in the rates of stump cancer. Dodds and Latour[7] disclosed a general incidence of 7.53 per cent and found that most cases develop between 5 and 32 years following the original operation. Hahn[13] reported a 9.7 per cent increase in 319 patients at the Oncologic Hospital.

Complications

To undertake this type of surgery involves the acceptance of a calculated risk by the patient and the surgeon. A high rate of surgical complications is unavoidable by the very nature of the procedure. Brunschwig[5] stated, "When the incidence of fistula is negligible in any series of patients the operations carried out were not as extensive as they might be." Rea,[22] discussing the technical difficulties of radical hysterectomy, lists urinary tract injury, vascular and nerve complications, rectal injuries, and postoperative shock as the problems of most frequent occurrence. It is a trite observation to state that the clinical extent of the disease increases the technical difficulty of the operation. The question has often been raised as to whether irradiation further increases the problems of operative technique. In a previous study of the effect of preoperative irradiation on endometrial carcinoma we[25] found that, when the disease was controlled, little was added to the surgical problem. This, however, is not truly a comparable situation, although Meigs[18] stated that he felt radiation had little effect on the frequency of fistulas in one series reported. Bastiaanse[28] feels that the difficulties involved in Schauta's operation are not increased by preoperative radium although lymphadenectomy is rendered more difficult by preoperative irradiation in Wertheim procedures.

The influence of irradiation in our series is evident in Table V. The cases subjected to hysterectomy and node dissection experienced a 40 per cent surgical complication rate. The incidence of these injuries was three times as frequent, however, in the patients previously treated by irradiation. The urinary tract was involved in most instances—10 out of 18 times, or a rate of 14.4 per cent in the 69 cases. Our occurrence of fistulas was 11 per cent, with ureteral and vaginal fistulas approximately equally distributed. Liu and Meigs[17] had a 9 per cent fistula rate with three fourths involving the ureter. Brunschwig,[5] reporting a series of 212 cases which included postradiation recurrences, had a 23.5 per cent incidence of urinary tract fistulas equally distributed between the ureter and bladder. In our series, no primary reparative procedures were performed on the recognized ureteral injuries. These cases were treated by ureterosigmoidostomy.

The major complications in the exenteration group are listed in Table VI and depended mainly upon the direction of the extirpation.

TABLE V. COMPLICATIONS FOLLOWING RADICAL HYSTERECTOMY

In 45 Patients With Previous Irradiation.—		
Vesicovaginal fistula (one with recurrence)	3	
Ureterovaginal fistula	2	
Postoperative evisceration	1	
Partial ureteral obstruction	1	
Rectovaginal fistula (one with recurrence)	2	
Ureterosigmoidostomy (1 because of disease; 1 surgical injury)	2	
Recto- and ureterovaginal fistula	1	
Wound abscess with possible endocarditis	1	
Total	13	(30%)
In 24 Patients With No Previous Irradiation.—		
Ureterovaginal fistula, nephrectomy	1	
Postoperative evisceration	1	
Lower nephron nephrosis	1	
Ureterosigmoidostomy (surgical injury in stump carcinoma)	1	
Ureteral injury, surgical; healed spontaneously	1	
Total	5	(11%)

TABLE VI. COMPLICATIONS FOLLOWING 35 EXENTERATIONS

Fistulas	6	(17.1%)
1 vesicovaginal, closed. Dead kidney		
1 ileovaginal, bowel resection. Patient living and well		
3 rectovaginal, 2 closed; 1 draining 4 months postoperatively		
1 bilateral ureterovaginal fistula. Patient died 60 days postoperatively from pyelonephritis with uremia		
Jaundice	2	
Superficial thrombophlebitis	1	
Pneumonia	1	
Total	10	(28.6%)

Results

The calculated risk of radical surgery is emphasized by the high hospital mortality rates. Death occurs in direct proportion to the extent of the operation performed. Only 2 patients (2.9 per cent) were lost in the hysterectomy group, one as a result of hemorrhage and shock 30 hours postoperatively, and one from the hepatorenal syndrome on the ninth postoperative day. Seventeen patients (33 per cent) were lost from the exenteration series. The associated causes of death are listed in Table VII.

TABLE VII. OPERATIVE MORTALITY FOLLOWING EXENTERATION

Total number of deaths in the hospital	17	(33.3%)
Anterior exenterations		5 (25.0%)
Posterior exenterations		3 (17.9%)
Total exenterations		9 (64.3%)
Causes of death:		
Pyelonephritis	5	
Toxic hepatitis, cardiac failure	1	
Anesthesia	2	
Rheumatic heart disease, cardiac failure	1	
Hepatorenal syndrome	2	
Hemorrhage	2	
Shock	1	
Uremia	1	
Pulmonary embolus	1	
Peritonitis, intestinal obstruction	1	
Total	17	

The total procedure accounts for twice as many deaths as the anterior exenteration and is three times as fatal as the posterior exenteration. The most frequent single cause of death is always complications associated with the

urinary tract. The length of survival of patients following radical procedures is dependent upon so many variables that comparative analyses are difficult and misleading. Parsons[21] found the average survival to be 16 months. His series experienced a 34 per cent hospital mortality and a 2 year survival rate of 33 to 45 per cent, depending upon the magnitude of the operation. Brunschwig[4] reported a 5 year survival of 12 per cent. When due consideration is given to the manifold difficulties involved in these cases, the results are surprisingly good.

Table VIII shows that well over one half of the patients requiring extirpation of the genital organs only may be expected to survive 2 to 5 years. In the more radical group, however, the outlook is more gloomy. Only one fourth of these patients have any expectancy of reasonable survival (Table IX).

TABLE VIII. SURVIVAL RATES IN 69 CASES OF RADICAL HYSTERECTOMY AND NODE DISSECTION

Operation 5 years ago		22
Living	10	
Dead in 2 years	7	
Dead in 2 to 5 years	5	
Operation 2 to 5 years ago		17
Living 2 years	14	
Dead in 2 years	3	
Surgery less than 2 years ago		30
		69
No. surviving 2 to 5 years (29 of 39) 74.3%		

TABLE IX. SURVIVAL RATES IN 50 CASES OF TOTAL OR PARTIAL EXENTERATION

Operation 5 years ago		11
Living	3 (27.2%)	
Dead in 2 years	8	
Operation 2 to 5 years ago		23
Living 2 years	5	
Dead in 2 years	18	
Operation less than 2 years ago		17
		51
Patients living 2 to 5 years (8 of 34 cases) 23.5%		

Comment

Any procedure which entails the technical proficiency and the high mortality risk of radical cancer surgery cannot be undertaken as a sideline. The problems of anesthesia, shock prevention, electrolyte balance, and antisepsis are so profoundly exaggerated under the circumstances that the successful outcome of any case involves the application of many talents. Defeat may come despite heroic and apparently adequate effort. It must constantly be borne in mind that one is dealing with an already seriously compromised physiology in the surgical candidates.

In the routine preoperative workup, it has been noted that a variety of upper urinary tract lesions are present in almost half the cases as seen in Table X. Failure or sepsis of the urinary tract accounted for most of the deaths. Urinary diversion operations seem to cause a higher mortality than unintentional injury to the urinary tract. Everett,[8] discussing ureteral transplant in cases of cancer of the female pelvis, reported an operative death rate of 43 per cent. To accommodate the diverted urinary excretion is an individual surgical problem of great magnitude. As yet, we have been unable to establish

the superiority of the Gilchrist or the Bricker pouch or the wet colostomy. All seem to have their advantages and liabilities. We have found urinary tract failure the cause of eventual death in a large proportion of the cases. Both Morton[19] and Ward[30] have reported this in the study of the causes of death in cervix cancer.

TABLE X. STATUS OF THE UPPER URINARY TRACT

Bilateral hydronephrosis	8%
Unilateral hydronephrosis	16%
Unilateral hydronephrosis with nonfunctioning other kidney	10%
Unilateral nonfunctioning kidney, other kidney normal	10%
Total urinary involvement	44%

Another variable which influences outcome is the microscopic extension of the disease. Table XI depicts the effect of extension of the disease beyond a clearly localized lesion as resulting in a disease of entirely different character. This, of course, has been a clinical observation of ours[24] of long standing, and it is regrettable that this concept has been omitted from the classifications currently in vogue. In 45 cases of hysterectomy and node dissection done for recurrent or resistant disease, positive nodes were determined in 13 instances. Three of these patients (23 per cent) are living and well. Meigs[17] had a 35 per cent 5 year survival in cases of positive nodes, and 81 per cent in those with negative nodes.

TABLE XI. CORRELATION OF SURVIVAL AND EXTENT OF DISEASE FOLLOWING RADICAL HYSTERECTOMY OVER 5 YEARS AGO

Living 5 Years.—	
Less than entire cervix	9
Entire cervix	0
Extension beyond cervix but not involving nodes	1
Node involvement	0
Dead Before 5 Years.—	
Less than entire cervix	1
Entire cervix	5
Extension beyond cervix but not involving nodes	4
Node involvement	2

We were unable to demonstrate any consistent effect of the time interval between irradiation and surgery. Table XII shows an irratic distribution of survival in this regard.

TABLE XII. EFFECT OF TIME INTERVAL BETWEEN RADIOTHERAPY AND SURGERY ON SURVIVAL

INTERVAL IN YEARS	% SURVIVING AVERAGE TIME
Exenterations.—	
Less than ½	9
½ to 1	18
1 to 1½	None
1½ to 2½	16.6
Over 2½	None
Radical Hysterectomy.—	
Less than ½	64
½ to 1	43
1 to 1½	60
1½ to 2½	57
Over 2½	2 patients, both living

Conclusions

The patient suffering from recurrent or persistent carcinoma of the cervix presents a challenge to the imagination, judgment, and technical skill of the cancer therapist. The brightest hope for the future lies in the development of a laboratory means of determining the presence of radioresistance prior to any therapy. Present-day surgical methods have enabled us to improve the salvage in cases of resistant disease rather than to depend on reirradiation or palliative procedures. By taking cognizance of the inevitable outcome inherent in these problems, time becomes of paramount importance to the patient. We must justify the high mortality, morbidity, and disability rates by affording a reasonable prognosis for useful living for acceptable periods of time. In Table XIII is the net expectancy that we may offer any given patient who enlists our aid. We can say, in effect, that approximately one half of the women accepting the risks of radical surgery can expect at least two years of additional life.

TABLE XIII. COMBINED SALVAGE IN 73 OPERATIONS 2 TO 5 YEARS AGO. SOME AS PRIMARY TREATMENT, SOME PALLIATIVE

OPERATION	NO. OF PATIENTS	NO. LIVING 2 TO 5 YEARS
Hysterectomy	39	29
Exenteration	34	8
Total	73	37 (50%)

Summary

1. One hundred and twenty patients, including 80 who had previously been irradiated, were subjected to definitive surgery.

2. Surgical injuries were three times as common in the previously irradiated patients.

3. Mortality rates were in direct proportion to the magnitude of the surgery undertaken.

4. When the lesion is clearly localized to the cervix the prognosis for 5 year survival is excellent.

5. The 2 to 5 year salvage in all types of exenteration was determined as 23.5 per cent.

6. The 2 to 5 year salvage rate in cases treated by extirpation of the genital organs alone was 74.3 per cent.

7. The hospital mortality rate in 51 exenteration cases was 33.3 per cent.

8. The status and recovery of the upper urinary tract profoundly influence survival rates.

References

1. Allen, W. M., Sherman, A. I., and Arneson, A. N.: AM. J. OBST. & GYNEC. 68: 1433, 1954.
2. Allen, W. M., Sherman, A. I., and Arneson, A. N.: AM. J. OBST. & GYNEC. 70: 786, 1955.
3. Beecham, C. T.: Obst. & Gynec. 8: 420, 1956.
4. Brunschwig, A., and Daniel, W.: Surg., Gynec. & Obst. 99: 324, 1954.
5. Brunschwig, A., and Frick, H. C., II: AM. J. OBST. & GYNEC. 72: 479, 1956.
6. Calkins, L. A.: South. M. J. 41: 902, 1948.
7. Dodds, J. R., and Latour, J. P. A.: AM. J. OBST. & GYNEC. 69: 252, 1955.
8. Everett, H. S., and Hill, H. M.: AM. J. OBST. & GYNEC. 68: 1279, 1954.

9. Glucksman, A., and Way, S. J.: J. Obst. & Gynaec. Brit. Emp. 55: 513, 1948.
10. Graham, J. B., Graham, R. M., and Liu, W.: Surg., Gynec. & Obst. 99: 555, 1954.
11. Graham, J. B., and Meigs, J. V.: AM. J. OBST. & GYNEC. 64: 908, 1952.
12. Gusberg, S. B.: AM. J. OBST. & GYNEC. 72: 804, 1956.
13. Hahn, G. A.: AM. J. OBST. & GYNEC. 69: 48, 1955.
14. Heyman, J.: AM. J. OBST. & GYNEC. 69: 502, 1955.
15. Keettel, W. C., Brintwell, E. S., Randall, John H.: Journal Lancet 72: 283, 1955.
16. Liu, Winifred: AM. J. OBST. & GYNEC. 69: 299, 1955.
17. Liu, Winifred, and Meigs, J. V.: AM. J. OBST. & GYNEC. 69: 1, 1955.
18. Meigs, J. V.: AM. J. OBST. & GYNEC. 72: 467, 1956.
19. Morton, D. G., and Dignam, W.: AM. J. OBST. & GYNEC. 64: 999, 1952.
20. Novak, E. R.: Obst. & Gynec. 4: 251, 1954.
21. Parsons, L., and Taymor, M.: AM. J. OBST. & GYNEC. 70: 774, 1955.
22. Rea, D. H.: AM. J. OBST. & GYNEC. 71: 764, 1956.
23. Read, C. D.: AM. J. OBST. & GYNEC. 56: 121, 1948.
24. Schmitz, H. E., and Nelson, P. A.: Am. J. Roentgenol. 45: 395, 1941.
25. Schmitz, H. E., Smith, C. J., and Gajewski, C. J.: AM. J. OBST. & GYNEC. 64: 952, 1952.
26. Smith, C. J., Stepto, R. C., Schack, C. B., and Schmitz, H. E.: AM. J. OBST. & GYNEC. 73: 598, 1957.
27. Truelsen, F.: Carcinoma of the Uterine Cervix, London, 1949, H. K. Lewis & Co., Ltd.
28. Van Bouwdijk Bastiaanse, M. H.: AM. J. OBST. & GYNEC. 72: 100, 1956.
29. Van Henk, M., and Friche, R. E.: Am. J. Roentgenol. 73: 437, 1955.
30. Ward, S. V., Sellers, T. B., and David, J. T., Jr.: AM. J. OBST. & GYNEC. 63: 989, 1952.

"CHRONIC" ECTOPIC TUBAL PREGNANCY*

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IN RECENT years we have been impressed with the frequent occurrence of "chronic" ectopic tubal pregnancy in our practice. The condition has been referred to in the literature under various designations such as "chronic," "obscure," "delayed," and "occult tubal rupture."

Henderson and Bean[1] reviewed 302 cases and classified 91 of them as "acute" and 211 as "chronic." "Acute" in this report, meant that the patients were in shock, and "chronic" meant that they were not in shock. Johnson[2] reported on 245 patients with ruptured ectopic pregnancy and divided them into "acute manifest" with signs of internal hemorrhage (64 per cent) and "obscure latent" with the products of conception and hemorrhage walled off (36 per cent). Johnson also pointed out that the correct preoperative diagnosis was made in 94.6 per cent of the patients in the manifest group, whereas in the obscure group a correct diagnosis was made in only 76 per cent.

We feel that the division of cases of ectopic tubal pregnancy into (1) "acute" and (2) "chronic" is worth while as the two clinical entities are in keeping with the two pathologic processes. In the acute group, the rupture is abrupt in onset and is usually accompanied by severe pain and shock from blood loss. The abdominal and pelvic findings are those of intraperitoneal hemorrhage with spreading tenderness, rigidity, and distention. The acute case is rarely missed by the "ectopic-minded" physician. The patient with chronic ectopic pregnancy has pain, bleeds a little, and walls off the process within the pelvis. This sequence continues until the hemorrhage or inflammatory process in the hematoma becomes apparent to the clinician. The "chronic" ectopic pregnancy is confused most frequently with chronic salpingo-oophoritis and infected early abortion.

Krohn,[3] Beacham,[4] Johnson,[2] Greenhill,[5] and others feel that there is an increasing incidence of tubal pregnancy caused by the common usage of antibiotics in treating salpingitis. Tubal patency is being maintained in patients who formerly would have had complete tubal occlusion. The presence of a patent tubal lumen does not mean that normal tubal physiology is maintained. The disturbance of the function of the tubal ciliary cells, decrease in peristaltic activity, and creation of more blind folds undoubtedly delay the migration of

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the fertilized egg and predispose to tubal nidation. Since these changes are more marked in the distal one third of the tube and since the "chronic" ectopic pregnancy usually occurs in the terminal portion of the tube, it seems reasonable to conclude that antibiotic therapy may predispose to the more chronic or obscure forms of ectopic gestation.

The clinical material to be reviewed, though small, illustrates a trend that may be occurring at least in a rural community practice with a moderately high Negro clientele.

Source of Material

From Jan. 1, 1950, through Dec. 31, 1956, we have treated, in our practice at Lenoir Memorial Hospital, 43 patients with tubal pregnancy. The total deliveries in our practice during these seven years were 4,259. This is an incidence of one tubal pregnancy for every 99 deliveries.

These 43 cases were divided, on the basis of the clinical features, into 20 acute and 23 chronic. All of the patients with acute tubal rupture exhibited evidence of intraperitoneal hemorrhage and varying degrees of shock on admission. The 23 patients with "chronic" ectopic pregnancy presented themselves with clinical features simulating pelvic inflammatory disease rather than rupture of the Fallopian tube.

General Clinical Data

A classification by race showed 16 white patients and 27 Negro patients. In the 20 cases of acute rupture, 11 patients were white and 9 were Negro. In the 23 cases of chronic rupture, 5 patients were white and 18 were Negro. The higher incidence of chronic ectopic pregnancies in the Negro race is related to the higher incidence of salpingitis.

The *age* distribution was not significant. The mean age in the acute group was 27.6 years while the mean age in the chronic group was 29.8 years.

An analysis of the *length of gestation* showed no appreciable difference in the two groups. In the acute group, the average duration of pregnancy was 8.3 weeks. In the chronic group, the average duration of pregnancy was 7.6 weeks.

Duration of Illness.—In the acute group, there were 5 patients who had symptoms for less than 24 hours. The average duration of symptoms for this group was 12.4 days.

In the chronic group, the average duration of symptoms was 23.4 days. The length of illness on admission in the chronic group was twice as long as that of the acute group. This difference in duration of illness probably is related to the pathologic process of repeated leaking and walling off within the pelvis, exhibited by the patients with chronic ectopic pregnancy, in contrast to the rupture and fulminating hemorrhage seen in the acute group.

Symptoms and Signs.—In the diagnosis of tubal pregnancy the clinical symptoms and signs are the most important factors and take precedence over all laboratory procedures. Definite differences were noted in the diagnostic features of these two groups of patients.

Abdominal pain was the most common symptom and was present in all patients in both the acute and chronic groups. Twelve of the 20 patients with acute tubal rupture had had pain less than 24 hours, and the other 8 had complained of pain for an average duration of 11 days. Only 3 of the 23 patients with chronic tubal leakage had had pain less than 24 hours and 20 patients

had complained of pain for a mean duration of 16 days. A history of shoulder-girdle pain was obtained in 6 patients in the acute group and 9 patients in the chronic group. A history of rectal pain was elicited in 2 patients, one in each group.

Uterine bleeding was the next most common symptom in both groups. Twelve of the 20 patients in the acute group complained of vaginal bleeding on admission. Nineteen of the 23 patients in the chronic group complained of vaginal bleeding on admission. The average duration of bleeding in the acute group was 15 days, as compared to an average duration of 25 days in the chronic group. The difference in frequency and duration of bleeding in the two groups is plausible, if the onset of bleeding in ectopic pregnancy is considered to be initiated by the death of the embryo and the interruption of hormone production by the trophoblastic tissue.

Syncope occurred in 12 patients in the acute group. It had been present for an average duration of 6.3 hours. A history of syncope was elicited in only 6 patients in the chronic group, present for an average duration of 4.6 days.

Shock was much more common in the patient with acute tubal rupture. Twelve of the acute group showed some degree of shock when first seen. None in the chronic group exhibited clinical evidence of shock on admission. Six of these patients with chronic ectopic pregnancy did show signs of shock after repeated examinations during the period of hospital observation.

Abdominal tenderness was present in 19 of the 20 patients in the acute group on admission. The one patient who did not exhibit abdominal tenderness had an unruptured ectopic pregnancy. Twenty-two of the 23 patients in the chronic group exhibited tenderness on admission.

Abdominal distention was slightly more prevalent in the acute rupture group. This was attributed to the irritating influence of free blood in the peritoneal cavity.

Pelvic examination in the acute rupture group disclosed a definite *adnexal mass* in only 4 patients. Unilateral adnexal fullness was described in 5 patients and thickening in 2 patients. Nothing was palpable in the adnexa in 9 patients in the acute group. All 23 patients in the group with a chronic leaking rupture had palpable adnexal findings: definite mass 19, fullness 1, and thickening 3.

A *febrile response* was present more frequently in the chronic ectopic group. The temperature graph resembled that of patients with chronic salpingo-oophoritis.

TABLE I. USE OF COLPOTOMY IN DIAGNOSIS OF ECTOPIC PREGNANCY, 1950-1956

YEAR	TOTAL NO. OF COLPOTOMIES	DIAGNOSIS OF ECTOPIC PREGNANCY	
		POSITIVE	NEGATIVE
1950	2	2	0
1951	2	2	0
1952	7	5	2
1953	9	6	3
1954	9	5	4
1955	8*	3	5
1956	11	5	6
Total	48	28†	20

*Culdocentesis, 2.

†Acute rupture of tube, 12; chronic rupture of tube, 16.

Diagnostic Measures.—The most important diagnostic aid was posterior colpotomy. During the 7 years of study, 48 colpotomies were done in an effort to diagnose tubal pregnancy. Twenty-eight of these were positive for ectopic pregnancy and 20 were negative. The posterior colpotomy was employed as an effort in diagnosis 12 times in the group with acute tubal rupture and 16

times in the chronic group. Only 2 laparotomies were done as a definitive diagnostic measure in the 48 patients submitted to colpotomy. Neither of these patients had ectopic pregnancies.

In a suspected tubal pregnancy posterior colpotomy will give a definitive diagnosis in most instances and without the trauma and increased hazards of celiotomy. This is in keeping with the views of Caldwell,[6] Thomas,[7] Bradbury,[8] and others. Exploration through the posterior cul-de-sac to differentiate between a chronic tubal pregnancy and an inflammatory process has proved to be invaluable in our experience.

The presence of anemia as evidenced by serial blood counts and hematocrit studies was a helpful adjunct in diagnosis. Leukocyte counts with differential studies, and sedimentation rates were determined on the majority of the patients in the chronic ectopic group but were of little value in distinguishing between ectopic pregnancy and chronic adnexitis. Biologic pregnancy tests were of value only when positive.

Operative Procedures.—Salpingectomy only was performed on 13 of the 20 patients with acute rupture of the tube. Two patients had salpingectomy and resection of the ovary. Two patients had salpingo-oophorectomy. Of the 2 patients with cornual rupture, one had a cornual resection and the other had a total abdominal hysterectomy. One patient was admitted in extremis and died before operation could be performed.

Salpingectomy only was performed on 9 patients of 23 with chronic rupture of the tube. Eleven patients had salpingo-oophorectomy. In 3 cases a total abdominal hysterectomy was done with salpingo-oophorectomy.

The more extensive operative procedures employed in the chronic ectopic group were necessary because of the increased destruction and distortion of the adnexal and pelvic tissues.

TABLE II. PATHOLOGIC FINDINGS IN 43 CASES OF TUBAL PREGNANCY

DESCRIPTION	ACUTE RUPTURE* (20)	CHRONIC RUPTURE (23)
Infection:		
Gross	10	23
Microscopic	5	12
Clean rupture	8	0
Walled-off mass	1	15
Site:		
Cornual	3	0
Isthmial	6	0
Outer one third	4	13
Not located	7	10
Omental adhesions	0	8

*One patient in acute group had unruptured tubal pregnancy.

Morbidity and Mortality.—The morbidity was higher in the chronic ectopic group. This was characterized by a higher incidence of postoperative fever, peritonitis, and paralytic ileus. These complications were managed conservatively. There were no wound disruptions and no diagnosed cases of thromboembolic disease.

There were 2 maternal deaths in the 43 cases of tubal pregnancy. One patient was admitted in extremis with acute rupture and massive intra-abdominal hemorrhage. This patient died before operation could be performed. The postmortem examination disclosed a massive cornual rupture. The other patient had a chronic tubal rupture with a large, adherent, necrotic, bleeding, right pelvic mass. The removal of the mass produced a large denuded area on the posterolateral pelvic wall in the region of the hypogastric and presacral venous plexuses, which continued to ooze despite all operative measures and multiple trans-

fusions. The patient died of irreversible shock 12 hours after operation. Early and intensive packing, with yards of 2 inch gauze, has proved helpful in the control of venous bleeding in this particular pelvic site.

Pathology.—Studies of gross and microscopic pathology were done on all patients. The descriptive features are illustrated in Table II. In the chronic rupture group, the ectopic mass and blood clots were completely walled off in 15 patients and the identified site of the rupture was in the outer one third of the tube in 13 patients. Three of these were classified as tubal abortions.

Summary

"Chronic" tubal pregnancy has accounted for over one half of the ectopic pregnancies seen in our private practice during the past 7 years.

The chronic rupture of the oviduct occurred most frequently in the multiparous Negro patient. The length of gestation was not increased, but the duration of illness was twice as long. None of the patients with chronic ectopic pregnancy exhibited evidence of shock on admission.

The demonstration of anemia was the only helpful laboratory study.

Posterior colpotomy was an invaluable diagnostic aid in differentiating between a "chronic" ectopic pregnancy and salpingo-oophoritis.

The pathologic process is usually that of a large infected walled-off hematoma around the products of conception in the outer one half of the Fallopian tube.

References

1. Henderson, D. N., and Bean, J. L.: Am. J. Obst. & Gynec. 59: 1225, 1950.
2. Johnson, W. O.: Am. J. Obst. & Gynec. 64: 1102, 1952.
3. Krohn, L., Priver, M. S., and Gotlib, M. H.: J. A. M. A. 150: 1291, 1952.
4. Beacham, W. D., et al: J. Missouri M. A. 48: 629, 1951.
5. Greenhill, J. P.: The 1955-1956 Year Book of Obstetrics and Gynecology, Chicago, 1956, The Year Book Publishers, Inc., p. 39.
6. Caldwell, J.: Am. J. Obst. & Gynec. 72: 1227, 1956.
7. Thomas, W. L.: J. Florida M. A. 41: 267, 1954.
8. Bradbury, W. C.: West. J. Surg. 60: 377, 1952.

Discussion

DR. FRANK R. SMITH, New York, N. Y.—There were two deaths in Dr. Parker's small series, one patient dead before operation could be performed, and one of shock 12 hours postoperatively, after severe hemorrhage had supposedly been controlled. If this control was actual, one wonders if blood replacement was complete. If so, could the shock 12 hours after operation be corticoadrenal shock? In the patient with oozing, vitamin K and C are of some value.

The racial incidence can be significant only if it is compared with the total population of the individual clinic.

Dr. Parker's choice of colpotomy to assist in making the diagnosis agrees completely with my own views. For most patients, in whom colpocentesis would be of value, the diagnosis is evident anyhow, although it may be worth while in differentiating between an ectopic pregnancy and a pelvic abscess. Even here a colpotomy would do just as well and eventually better, because it would be definitive treatment for the abscess. Unless blood or pus is immediately encountered, however, the full value of colpotomy is not attained unless both tubes and ovaries can be visualized. Culdoscopy is mentioned only to condemn it as meddlesome curiosity.

The author's feeling about the slight value of laboratory tests except those evaluating anemia is in agreement with my own experience. I would like, however, to point out that in 83 per cent of our so-called "chronic ectopics" flat plates showed significant findings.

The often-mentioned explanation that the increase in the incidence of ectopic pregnancies is due to previous antibiotic therapy for pelvic infection with resulting partial canalization of the tubes may be true, but there is reason to believe that the increased incidence is apparent rather than factual. At New York Lying-In Hospital there were 351 ectopic pregnancies during the years 1932-1955 (and 117 of these occurred in the 5 year period from 1951 to 1955), yet, in proportion to pregnancies in this clinic for the same years, there was little difference.

I would like to emphasize that, in a case of doubtful so-called "chronic ectopic," deterioration of the patient's status as noted by progressing anemia, increase or return of pain requires prompt surgical intervention, regardless of all other tests. The length of the postoperative hospital stay itself is definitely influenced by the delay in adequate treatment.

Kohl[1] and his co-workers in 1956 reported in an excellent article that in 454 consecutive ectopic pregnancies at Kings County Hospital in Brooklyn (1942-1951) the diagnosis was correct in 89 per cent of cases, with 6 deaths, or a mortality of 1.3 per cent. Yet Rosenthal[2] stated that in Brooklyn, New York, from 1937 to 1950 there were 64 maternal deaths from early ectopic gestation. The diagnosis was incorrect in 30 of the 64 cases or 47 per cent, and in 18 other cases delay in therapy was sufficiently long to cause death although tubal pregnancy was suspected.

References

1. Kohl, S. G., Trigone, V., and Siegler, A. M.: New York J. Med. 56: 850, 1956.
2. Rosenthal, A., and Glass, M.: New York J. Med. 51: 2493, 1951.

DR. THOMAS G. HERBERT, JR., Charleston, S. C.—Dr. Parker's paper presents statistical and clinical differences between the ectopic pregnancy that, as we often say, we may diagnose by telephone, and the obscure ectopic pregnancy that causes us worry and sleepless nights wondering just what will happen to the patient under observation.

To offer contrast with a private practice series, we reviewed the ectopic pregnancies that occurred on the ward service of the Roper Hospital during the years 1954-1956. The total number of cases for which we could find reliable records was 49; during that time there were 4,730 deliveries. Our cases also indicate a differentiation between the classic type of ectopic gestation and the obscure type. Statistically, our figures are somewhat at variance with Dr. Parker's in that out of our 49 cases only 16 were classifiable as obscure, amounting to some 32 per cent—nearer the figures quoted by Johnson. By and large, the remainder of our statistics coincide with those presented. Pelvic inflammatory disease occurred in 29 instances and, like the writer, we found pelvic inflammatory disease present in all of the obscure cases but 2.

These ectopic gestations were not successfully walled off, and even in the cases in which obscurity was noted sometimes there was a surprising amount of blood free in the abdominal cavity; in only a relatively few instances was a well-defined hematoma present. We agree that some type of cul-de-sac diagnostic penetration is invaluable in clarifying the obscure type of ectopic gestation. This belief is documented by the statistics indicating that cul-de-sac puncture was done in 41 of our 49 cases. This was done many times purely as a confirmatory procedure in an otherwise well-defined ectopic gestation. As a ward service procedure puncture of the cul-de-sac with the needle and local anesthesia has economic advantages over the more elaborate colpotomy. Thirty-nine of the 41 cul-de-sac punctures were positive, 2 were negative. Surgical delay in this series of ectopic pregnancies varied from almost none to as much as 10 days. It is of interest that in each instance of unusual delay, puncture of the cul-de-sac had either been omitted or much delayed.

Admitting the fact that many tubal abortions passed undiagnosed, I find the infrequency of this entity in Dr. Parker's series and in our own figures puzzling. Tubal abortion is stated

in the standard texts to be the most common mode of termination of ectopic pregnancy. Increased use of colpotomy, cul-de-sac puncture, or culdoscopy should increase the frequency with which this process is detected.

DR. H. HUDNALL WARE, JR., Richmond, Va.—The term "chronic ruptured tubal pregnancy" may not mean the same to all physicians, but if it helps to focus our attention on the leaking or old ruptured ectopic gestation, especially those of several days' or weeks' duration, it may prevent more prolonged delay or neglect of many of these patients, and decrease the mortality in this group.

The importance of ectopic gestation as a cause of maternal deaths may be emphasized by the fact that 9 (15 per cent) of the 59 maternal deaths in Virginia, in 1955, were due to ectopic gestation, a complication which usually occurs only once in 303 pregnancies. Most of the 9 deaths were due to delay in diagnosis or delay in operation, and failure to transfuse the patients early with sufficient whole blood.

At the Medical College of Virginia Hospitals, we rarely resort to needle aspiration of the cul-de-sac or colpotomy or similar procedures, and we have had one maternal death in the last 398 ectopic pregnancies.

DR. PARKER (Closing).—In answer to Dr. Smith's question concerning the transfusions received by the patient who died postoperatively, she received 3,500 c.c of whole citrated blood during the 12 hours after operation. The denuded, necrotic site on the posterior wall of the pelvis, as described, was oozing when the abdomen was closed, in spite of all methods that had been used to control the bleeding. We were of the opinion that this area continued to bleed, maintaining the irreversible shock. In similar cases that we have had since this death occurred, we have controlled the bleeding by packing the pelvis with gauze and removing the pack vaginally a few days later.

VAGINAL HYSTERECTOMY AFTER PREVIOUS PELVIC SURGERY*

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VAGINAL hysterectomy is now accepted by almost all gynecologists. There is still, however, no complete agreement on all of the indications, and more particularly on the contraindications. Probably the widest difference of opinion relates to whether or not previous pelvic surgery is a contraindication to vaginal hysterectomy.

All degrees of opinion have been given by experienced operators. Israel[1] listed previous pelvic surgery as a "relatively fixed" contraindication to vaginal hysterectomy. Payne[3] described previous surgery as "a commonly accepted contraindication to the vaginal approach." Banks and Rutherford,[4] who are credited with significant refinements in vaginal operative technique, regard previous surgery as an absolute contraindication. Counseller[5] advised "considerable caution" in selecting patients after previous surgery. Te Linde[6] considered that "previous pelvic surgery may or may not contraindicate vaginal removal of the uterus."

On the other hand, Brill and Golden[7] demonstrated in a large series of patients that vaginal hysterectomy was practical and safe after almost any type or extent of pelvic surgery. Their viewpoint was confirmed by the work of Leventhal and Lazarus[8] at Michael Reese Hospital, by the excellent results of Bradford[2] and of others. These and other equally divergent opinions from the literature show that the status of previous pelvic surgery as a contraindication to vaginal hysterectomy is far from settled.

The objectives of this discussion are threefold: (1) to point out and to summarize the wide diversity of opinion on the subject; (2) to strengthen the existing evidence that previous pelvic surgery rarely contraindicates vaginal hysterectomy; (3) to present the concept that previous pelvic surgery itself frequently provides an indication rather than a contraindication to vaginal hysterectomy.

Method of Study

The records of all patients on whom we performed vaginal hysterectomy between January, 1948, and October, 1956, were examined. These were private and service patients admitted to Duke Hospital, Colon Hospital,

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Panama Canal Zone, and the three general hospitals of Tampa.* Between 1948 and 1951, an occasional vaginal hysterectomy was not attempted by us because of previous pelvic surgery. After January, 1952, no previous pelvic surgery, regardless of type or extent, was considered a contraindication.

Material

Vaginal hysterectomy was performed by us on 274 patients. Seventy-one of these patients (26 per cent) had undergone previous pelvic surgery. These seventy-one patients had had a total of 116 gynecologic procedures. Ten patients had undergone two separate gynecologic operations, 3 patients had had three operations, and 2 patients had had four pelvic operations. These previous pelvic operations are summarized in Table I.

TABLE I. PREVIOUS PELVIC SURGERY IN PATIENTS TREATED BY VAGINAL HYSTERECTOMY

Round ligament suspension of the uterus	30
Excision or ligation of one or both tubes	29
Excision of one or both ovaries	14
Resection of ovarian cyst	9
Repair of cystocele	11
Cesarean section	6
Myomectomy	4
Trachelectomy	7
Ventral fixation of the uterus	3
Manchester operation	1
Colpotomy for abscess	2

Special Operative Problems

These studies confirm previous findings that uterine suspension, in spite of its rare use by most gynecologists, is still the most commonly performed pelvic operation. Diddle[9] found that uterine suspension accounted for 10 to 50 per cent of all gynecologic operations performed in five private hospitals in Tennessee. In this series, the majority of the patients who had had round ligament suspension still showed retroversion or descensus of the uterus, or both. Uterine suspension offered little if any difficulty to the performance of vaginal hysterectomy.

Ventral fixation, as demonstrated preoperatively by dimpling of the abdominal wall on traction of the cervix, had been performed in 3 patients. There is sufficient laxity of the abdominal wall in most multiparous patients to allow the site of fixation to be pulled into the operative field and separated under direct exposure. We felt that this approach from the uterine side was easier than a blind approach to the site of fixation through an old abdominal scar.

However, an unrecognized ventral fixation provided one of the 2 "failures" to accomplish hysterectomy per vaginam. This patient was an 82-year-old widow who thought she had had a total hysterectomy at the age of 45. On pelvic examination, she appeared to have a prolapse of the vaginal vault with a small dimple in the cuff. Under anesthesia, the dimple proved to be the cervix of an attenuated, tubular uterus, 15 cm. long and 1½ cm. thick, with fundus fixed to the abdominal wall. The lower part of the uterus was freed as high as could be visualized. The vaginal plastic work was done, then the upper portion of the uterus was removed through an abdominal incision. Both ovaries but not the uterus had been removed in her previous operation.

*Tampa General Hospital, St. Joseph's Hospital, and Clara Frye Memorial Hospital.

The second patient who required the abdominal approach was a 38-year-old para i, gravida i, who had had bilateral salpingectomy and right oophorectomy. A cystic adnexal mass was palpated preoperatively on the left. A vaginal hysterectomy was easily accomplished. The left infundibulopelvic ligament was found to be shortened and fibrous. The ovary was matted in omentum and adhesions. Vaginal removal was considered impractical. The cyst was easily removed by the abdominal approach and was reported by the laboratory as an endometrioma. Her recovery was uneventful.

The other previous operations provided no specific difficulties. In general, previous adnexal surgery offered the fewest adhesions. Previous repairs of cystocele produced some fibrosis but gave no real problem. Trachelectomy always left enough cervix to grasp carefully with the tenaculum. The Manchester procedure produced a thickened but otherwise normal parametrium.

We felt that, in all of these patients who had undergone previous surgery, the vaginal approach required absolutely no sacrifice of surgical exposure, of final hemostasis, of scope of operation, or of cure of symptoms. We agree with Thomas[10] that the difficulty and dangers of separating omental and intestinal adhesions per vaginam have been greatly exaggerated. In one patient of this series, a cyst of the omentum, measuring 10 cm. in diameter, was removed intact per vaginam with ease.

Comment

We propose that there is no "failure," in the true sense of the word, in the vaginal approach when the operator accomplishes vaginal repair and as much of the hysterectomy as is feasible per vaginam, then completes the operation by the abdominal approach. Usually the more difficult and more curative part of the operation will have been performed before the abdominal part is begun. Several English gynecologists have advocated first the vaginal dissection of the parametrium and lower broad ligament as a method of making difficult abdominal hysterectomy easier.

Of the 71 patients who had had previous pelvic surgery, 14 patients gave a clear-cut history of excessive or too frequent uterine bleeding beginning within six months after operation. All of these patients had had adnexal surgery, either bilateral or unilateral. The bleeding was of sufficient volume to warrant subsequent vaginal hysterectomy. At operation the remaining adnexa showed various degrees of degenerative changes, cysts, and adhesions. The uterus and endometrium in all were normal. Considering the time interval after operation, one could only conclude that the previous adnexal surgery had damaged ovarian function and had produced excessive bleeding. Thus, as far as could be reasonably determined, 20 per cent of the postoperative patients required vaginal hysterectomy for symptoms attributable to previous pelvic surgery. In these patients, we consider that previous pelvic surgery provided an indication rather than a contraindication to vaginal hysterectomy.

It is reasonable to anticipate that each year, as more good obstetrics is practiced, prolapse and relaxation will decline as an indication for vaginal hysterectomy. There is no such rosy outlook for the rapid limitation and decline of useless or poorly indicated pelvic surgery. The establishment of hospital Tissue Committees and medical Audit Committees and the restriction

of staff privileges has reduced, but by no means eliminated, this problem. A recent paper by Martzloff[11] on the frequency of "Ill-Advised Pelvic Surgery" is depressingly accurate. The work of Doyle[12] in California on unnecessary adnexal surgery and of Diddle[9] on unnecessary gynecologic surgery in Tennessee is even less encouraging. These papers show clearly that the problem of too much surgery is not confined to any locality, and that the decline of unnecessary surgery is painfully slow.

As pelvic relaxation declines as an indication for vaginal hysterectomy, pelvic surgery done with faulty technique or indications may well increase proportionately. The aftermath of needless surgery, both in failure of cure and in postoperative disturbance of function, will be a common problem to gynecologists for years to come. Previous pelvic surgery frequently will provide an indication for rather than a contraindication to vaginal hysterectomy.

Summary

1. The wide diversity of opinion on previous pelvic surgery as a contraindication to vaginal hysterectomy is summarized from the literature.

2. Seventy-one additional cases are reported in which vaginal hysterectomy was undertaken following previous pelvic surgery. Failure to accomplish vaginal hysterectomy occurred in 2 of these patients.

3. This series of cases confirms the existing evidence that vaginal hysterectomy after almost any type or extent of previous pelvic surgery is a practical and safe procedure.

4. The concept is presented that previous pelvic surgery itself frequently provides an indication for rather than a contraindication to vaginal hysterectomy.

References

1. Israel, S. Leon: Am. J. Obst. & Gynec. 69: 87, 1955.
2. Bradford, W. Z., Bradford, W. B., Woltz, J. H. E., and Brown, C. W.: Am. J. Obst. & Gynec. 68: 540, 1954.
3. Payne, Franklin L.: Discussion of Bradford et al.[2]
4. Banks, A. Lawrence, and Rutherford, Robert N.: West. J. Surg. 63: 23, 1955.
5. Counseller, V. S.: Obst. & Gynec. 1: 84, 1953.
6. Te Linde, Richard W.: Operative Gynecology, ed. 2, 1946, Philadelphia, J. B. Lippincott Company.
7. Brill, H. M., and Golden, M.: Am. J. Obst. & Gynec. 62: 528, 1951.
8. Leventhal, M. L., and Lazarus, M. L.: Am. J. Obst. & Gynec. 61: 289, 1951.
9. Diddle, A. W., O'Connor, K. A., and Winebrenner, J. D.: Obst. & Gynec. 1: 197, 1953.
10. Thomas, Walter L.: J. Florida M. A. 41: 267, 1954.
11. Martzloff, Karl: Northwest Med. 52: 1017, 1953.
12. Doyle, J. C.: J. A. M. A. 148: 1105, 1952.

Discussion

DR. PEMBROKE T. GROVE, Charleston, S. C.—After reading Dr. Ingram's paper I decided to check my experiences against his. I find, in reviewing 218 cases with a six months' follow-up of each and a minimum of two examinations, that my experience parallels his. I find, as he did, that as my technical proficiency improved, the selection of cases became broader.

Total cases		218
Vaginal hysterectomy with repair of anterior and posterior walls	87	
Vaginal hysterectomy with posterior colpoplasty	107	
Vaginal hysterectomy with vaginectomy	15	
Vaginal hysterectomy	9	
Previous lower abdominal surgery:		
Appendectomy		59
Adnexal operations:		
Unilateral		13
Bilateral		5
Suspension		13
Postpartum tubal resection		19
Adhesions		
Adnexal		21
Uterine		6
Results (symptomatically):		
Good		209
Fair		5
Poor		4

As a result of my experiences, I feel that the chief criterion to be met in selecting a case for vaginal hysterectomy is mobility of the uterus. Any condition that fixes the uterus, such as pelvic inflammatory disease, endometriosis, or mechanical fixation (for instance, ventral suspension) contraindicates this procedure. The hysterectomy should then be done by the abdominal route.

The visualization and the handling of the various adhesions presented no problem. After the uterus was dissected to the top of the fundus they were removed and ligated under direct vision.

Basically I agree with the author's observations and his conclusion that, in the hands of an experienced team, vaginal hysterectomy is a good procedure but not one for the occasional operator.

DR. WILLIAMSON Z. BRADFORD, Charlotte, N. C.—Dr. Ingram submits two major conclusions. The first of these deals with the technical problems of vaginal extirpation of the uterus subsequent to previous gynecological surgery. In 71 cases, or 26 per cent of his series, vaginal hysterectomy following previous pelvic surgery was elected with 2 failures requiring laparotomy. This incidence coincides closely with a similar study presented by the discussant to this society several years ago. It is apparent that previous pelvic surgery per se need not deter the gynecological surgeon from the operation of choice.

Possible difficulty may still be anticipated, however, by the surgeon with an open mind. Dr. Ingram does not discuss the special pathological findings noted at the time of previous pelvic surgery. An abdominal operation for pelvic endometriosis in the past, for instance, should have sobering implications in the election of vaginal hysterectomy, whereas a simple tubal sterilization need cause little concern.

Possible complications of previous surgery or pelvic lesions acquired at a later date also have a bearing upon the judicious choice of surgical procedure. If the former surgery has been complicated by pelvic peritonitis or has involved a ventral fixation, or if the patient has subsequently developed endometriosis of the cul-de-sac or pelvic inflammatory disease, in our opinion it is better judgment to use the abdominal exposure. Fortunately, this formidable array is seldom present and with Dr. Ingram I agree that ordinarily the previous operation does not present the problem with which it has been credited.

Concerning his second conclusion, there might be divergence of interpretation. The so-called inadequate or poorly indicated pelvic operation as an indication for hysterectomy is easier to accept than his conclusion that the avenue of approach should be per vaginam because of the previous surgery. Certainly the conclusion that poorly chosen surgery is followed frequently by malfunctioning of the uterus, dysmenorrhea, or pelvic disability is worthy of re-emphasis and with this we heartily agree.

I wish to offer the following criteria for vaginal approach in the secondary pelvic operation: first, symptomatic pelvic relaxation requiring repair; second, mobility of the cervix and parametrium with accessibility of the corpus; and, last, the presence of persistent pelvic disability not responding to more conservative therapeutic measures.

DR. A. D. CAMPBELL, Montreal, Quebec.—In recent years, vaginal hysterectomy has become quite popular. I feel that probably the pendulum has swung somewhat blindly in favor of this procedure. By and large, gynecological surgery is divided into the surgical treatment of pelvic lesions which naturally should be approached through an abdominal incision, and vaginal surgery. The indications for both are fairly well delineated. Whether in pelvic or vaginal surgery, there are certain surgical principles to which we must adhere, namely: (1) One must have adequate exposure. (2) One must preserve normal tissue. (If the vagina is not relaxed, in performing a vaginal hysterectomy, the normal vagina and its supporting structures must be incised.) (3) One must avoid unnecessary trauma. (4) One must avoid excessive blood loss. (5) One must reconstruct all structures as anatomically as possible. (6) All deperitonized areas must be perfectly reperitonized.

If vaginal hysterectomy is elected in the presence of pelvic inflammatory disease, endometriosis, and extensive adhesions, I submit that one cannot conform to the above axioms. In general, vaginal hysterectomy should be considered only when the uterus is movable, when it is no longer than the size of a 2 months' pregnancy, and when not involved in adhesions.

I suggest, therefore, that if we are to conform to all the surgical principles, we should individualize our cases and not try to remove the uterus vaginally if any pelvic lesions are suspected or when it is felt that such a procedure cannot be carried out with reasonable ease. If, on the other hand, one suspects adhesions to the uterus, the adnexa, or between loops of bowel, one should bring the pelvic basin and its contents into direct view. Obviously, one cannot do so by the vaginal approach.

Dr. Ingram's paper is very stimulating. Having removed fibroid uteri, ovarian cysts, ventrally suspended uteri, and even the appendix from below, I am convinced that here the vaginal approach is not commendable. I consider it a mechanical accomplishment—but not good surgery. On the other hand, if there is a very considerable degree of relaxation of the supporting structures of the pelvic organs, one may hope to remove the uterus vaginally for, in so doing, one will obviate a double procedure and at the same time reconstruct the birth canal and its supports.

In brief, I feel that vaginal hysterectomy should be confined to a relatively limited field.

DR. INGRAM (Closing).—It was mentioned that the entire operating team should be experienced before any vaginal hysterectomy is undertaken. We believe that there is no operation in gynecology other than vaginal hysterectomy in which the assistants are just as important as or more important than the operators. We do not attempt vaginal hysterectomy, particularly when a tedious operation is attempted, unless one of our partners is first assistant. We follow the precepts of Dr. Campbell and Dr. Davis in having a good spotlight, our own Heaney clamps, and our own retractors. A chair with a nice thick cushion and a back also increases the efficiency and comfort of the operator.

We agree that if there is an absolute contraindication for vaginal hysterectomy it is endometriosis. We do not attempt a vaginal hysterectomy with a preoperative diagnosis of endometriosis. Infection, we believe, is overrated as a contraindication. Most adhesions following infection can be separated easily. The antibiotics have greatly reduced the degree of pelvic immobilization due to infection.

Dr. Campbell mentioned the limitations of vaginal hysterectomy. This paper is not intended to push vaginal hysterectomy beyond its logical limitations. We do not attempt to deal with large tumors or adnexal disease by the vaginal approach. This paper is presented in the belief that previous pelvic surgery is the most overrated contraindication to vaginal hysterectomy.

TREATMENT AND PROGNOSIS IN CANCER OF THE OVARY*

With a Review of a New Series of 143 Cases Treated in the Years 1944-1951

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IN INTRODUCTION to the subject of carcinoma of the ovary, a brief word must be said about incidence and the possibilities of early diagnosis. Statistics of general cancer incidence in the United States show that although the ovary is one of the less common sites for primary cancer in the female reproductive tract, ovarian cancer is the only one in which an increase in the incidence appears to be taking place. Indeed, with cancer of the respiratory organs and pancreas, it is one of the few forms of cancer in women which seems to have shown an absolute increase in frequency, when due allowance is made for the increasing average age of the American population.

Of great importance in one's evaluation of the problem of early diagnosis are the figures published by Randall and Gerhardt[1] on the probability of eventual development of ovarian cancer at any given age in a woman's life. Their figures show that the chance of carcinoma of the ovary subsequently appearing is nearly 1 per cent in a woman of 40 (.930) and thereafter gradually diminishes.

Although we must certainly continue to urge routine examinations for the early detection of cancer of the breast and uterus and must certainly include palpation of the ovary as part of this routine, the gynecologist may expect to detect symptomless cancer of the ovary only once or twice in his entire career. Less than 2 per cent of patients in our previous series[2] were without symptoms. These considerations, if any additional arguments were needed, seem to emphasize the importance of therapy and its proper evaluation in the problem of cancer of the ovary.

In 1949, two of us[3] published a review with end results of the cases of cancer of the ovary treated at the Sloane Hospital during the period from 1922 to 1943. In this series there were 200 cases of primary cancer and 53 metastatic tumors of the ovary. The 5 year cure rate for the cases of primary cancer during this period was 27.5 per cent. This was a relatively good figure,

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but the authors were quick to admit that the precise figure reported in any article was at least as dependent upon the pathological criteria for malignancy and the categories included as upon any actual or claimed excellence of treatment.

For the further study of this problem, we now have an additional 148 cases of primary cancer treated during the years 1944-1951, inclusive, for which 5 year end results are available. These new cases with the older series give us a total of 343 cases of primary cancer of the ovary treated at least 5 years ago. On the basis of these new cases, we propose to re-examine the subject and to determine whether any significant improvement in therapy has been accomplished.

I. Classification of Ovarian Tumors in Relation to Prognosis

Statistics on ovarian carcinoma have been notoriously unreliable and perhaps for that reason have been of relatively little interest to the gynecologists. In the 1949 article by Munnell and Taylor,[3] statistics reported by various authors were summarized in a table which gave 5 year cure rates varying from 6.3 per cent to 65.4 per cent. With gynecologists arguing bitterly over differences of a few per cent in cases of cancer of the cervix it was small wonder that such reported figures for carcinoma of the ovary should be viewed with indifference. Later it will be shown that recent reports on end results for cancer of the ovary have become much more consistent.

End results are of little importance in themselves, but of enormous significance as a measure of the relative success or failure of a method of treatment. For this reason it is essential that efforts constantly be made to refine methods of classification so that end results may be meaningful.

In carcinoma of the ovary, the problem of finding a classification of cases which will set up homogeneous groups within which the only variable is the method of therapy is peculiarly difficult. These difficulties are based on the heterogeneous nature of ovarian cancer when viewed as a whole, the variables being the following: (1) the histogenetic origin of the tumor, for as is well known there are many sources of ovarian malignancy; (2) the histological degree of tissue differentiation, for it appears that the grade of malignancy plays a more important role in cancer of the ovary than in most other organs; (3) the clinical extent of the disease, for the stage of advancement at which treatment is instituted is apt to be less favorable, and the percentage of early cases more variable from one clinic to another, in cancer of the ovary than for at least any other kind of gynecological cancer.

A subdivision of cases of cancer of the ovary into more or less homogeneous subgroups according to these criteria is essential if we are to isolate and study the effects of therapy. Such subdivision results in very small groups, but opinions based on such small numbers are better than those based on larger collections that are heterogeneous. Consideration of these criteria for subdivisions must next be considered.

A. The Histogenetic Types of Ovarian Cancer.—

Primary tumors of the ovary may be classified according to origin by the recognition of four simple groups, namely, the epithelial tumors, the connective-tissue tumors, the mixed tumors, and the tumors of specific gonadal cells, the so-called dysontogenetic tumors.

Of these, the serous papillary tumors supply, in our experience, about 70 per cent of the cancers, the pseudomucinous tumors another 10 per cent. Some

8 per cent of all ovarian cancers belong to one of the several rarer varieties. About 12 per cent are unidentifiable by any means at our disposal at present, some of these being perhaps metastatic from an unknown source outside of the pelvis.

Series of cases upon which end results are reported will be based largely on cases of papillary serous and pseudomucinous cystadenocarcinoma and the figure for the percentage of cures will depend to a large extent upon the results achieved in these types. However, the inclusion of other forms will influence these figures to some extent and, in general, for the better.

The histological criteria of malignancy in granulosa-cell tumors are very uncertain and it is perhaps best for the clinician to regard them all as malignant. On the basis of observed recurrences, however, only 23 per cent of all granulosa-cell tumors treated in our hospital have proved to be malignant. In a similar series, Henderson[4] reported known recurrences in 25 per cent. The treacherous character of these tumors is shown by the fact that 2 cases of our series classed as benign, from microscopic examination, recurred, one 2 years, and one 18 years after initial treatment.[5]

B. Degree of Differentiation in Ovarian Tumors.—

Differences in the course or, more precisely, in the total life history of cancers arising even in the same tissues are a commonplace of clinical observation. That these differences are dependent upon biochemical and biological factors seems evident, and it has been the hope of many students of cancer that dependable morphological criteria could be found that would make the course of the disease more predictable.

Experience with grading of cervical cancer has in general led the gynecologist to a position of skepticism about the value of the effort. The papillary tumors of the ovary, on the contrary, are in our opinion amenable to successful classification with regard to their degree of malignancy. Indeed, such a classification is essential for their practical prognosis.

The reasons why grading is successful in papillary ovarian tumors, while failing in the epidermoid variety, are several. First of all, when looking at the microscopic preparations of a cancer of the cervix one is nearly always observing areas of invading cancer, in which the intrinsic structure of the tumor is modified by the effects of the immediately surrounding tissue environment. In the papillary tumors of the ovary, on the other hand, one can find areas of freely growing papillomas projecting into cystic cavities, and presenting the structure of the tumor in its natural form, unaffected by other influences. The grading of cancers of the cervix is further made difficult by the natural tendency of epidermoid cells to evolve from the small active basal cells to large, keratinized cells of the surface. This mixture of cells, dependent upon the normal behavior of squamous epithelium, is easily confused with the abnormalities of size, shape, and staining reaction supposedly characteristic of anaplasia. The structure of cancer of the ovary is complicated by no such physiological mixture of cell forms.

The papillary tumors of the ovary, both the serous and pseudomucinous varieties, must therefore be graded. One may recognize, at the very least, types that are almost certainly benign, others that are surely malignant. Besides these there are many cases in which the histology must be called "borderline." In regard to this intermediate group opinions of even the most experienced will differ. The results in such "borderline" cases will in fact be favorable in a very high percentage of instances, but an occasional late recurrence attests the potentiality of danger.

There is no doubt, then, that the classification of the various papillary tumors with regard to grade is essential in prognosis, and does in fact determine to a large extent the end result figures that are reported. In describing our own results, reference will repeatedly be made to the effect on the figures of the inclusion or exclusion of this group with a "borderline" histology.

C. The Extent of the Disease.—

It is still obvious that the most important single factor in the curability of an individual case of cancer of the ovary is the extent of the disease at the time that operation is undertaken. This is of course not an entirely independent factor, because the tendency to spread within a given period of time is itself related to the histogenetic type of cell from which the tumor is derived and also upon the degree of malignancy inherent in the tumor. Nevertheless, from a practical standpoint, the observed amount of dissemination is the factor upon which the clinician depends the most in making a prognosis.

In the report of 1949, a classification based on four stages was proposed and this will be followed in the present report also. It appears to us to be a practical and valid one, since it is not only a pathological description, but conforms to some of the necessities of therapy. It is summarized in Table I.

TABLE I. CLASSIFICATION OF CASES OF OVARIAN CARCINOMA ACCORDING TO EXTENT OF DISEASE

Stage I	Cancer limited to one ovary only
Stage II	Cancer limited to both ovaries
Stage III	Cancer extended to involve other pelvic viscera or peritoneum
Stage IV	Cancer extended to upper abdomen, peritoneum, viscera, or omentum

II. End Results for the Years 1944 Through 1951

The patients treated in the years 1944 through 1951 were studied to determine whether the results of treatment were better than for the earlier period already reported.

Methods of treatment had changed only slightly. In the earlier period there were more cases in which no postoperative x-ray therapy was given, and more in which x-ray therapy was administered with machines of relatively lower voltage, such as 180 kv., and lower dosage. During the 1944-1951 era, most patients received some postoperative therapy and the 250 kv. type of machine came into use. Total dosage was still low by modern standards. The comparison of the two epochs will serve then to show what a greater consciousness of the problem and a slightly improved technique of radiation may accomplish. It does not serve to test any entirely new principles.

TABLE II. FIVE-YEAR END RESULTS IN 148 CASES OF PRIMARY OVARIAN CARCINOMA FROM 1944 THROUGH 1951

	A	B		C	D	D/C	D/A
		LOST TO FOLLOW-UP					
	TOTAL CASES	B1 WELL WHEN LOST	B2 PROBABLY DEAD	DETERMINATE REMAINDER A-B1	5 YEAR SURVIVORS	RELATIVE 5 YEAR SURVIVAL RATE (%)	ABSOLUTE 5 YEAR SURVIVAL RATE (%)
Papillary serous cystadenocarcinoma	105	4	3	101	25	24.7	23.8
Papillary pseudomucinous cystadenocarcinoma	15	2	1	13	8	61.1	53.3
Granulosa-cell carcinoma	10	2	–	8	7	80.0	70.0
Undifferentiated adenocarcinoma	8	0	0	8	0	0	0
Unclassifiable carcinoma	10	1	1	9	1	11.0	10.0
Total	148	9	5	139	41	29.4	27.7

In the new series (Table II), the absolute 5 year survival rate was 27.7 per cent, which is almost identical with the figure of 27.5 per cent reported for our previous series. This figure falls in the general range noted by other clinics[6-15] reporting their results during the same period of time (Table III).

TABLE III. END RESULTS IN CANCER OF THE OVARY REPORTED BY OTHER AUTHORS, 1949-1957

AUTHOR	PERCENTAGE OF 5 YEAR CURES	YEAR OF REPORT
Munnell and Taylor[3]	27.5	1949
Allan and Hertig[6]	35.0	1949
Schmitz and Majewski[7]	20.3	1951
Wheelock, Fennell, and Meigs[8]	26.6	1951
Kerr and Elkins[9]	30.4	1951
Randall and Hall[10]	14.4; 6.4	1952
Javert and Roscoe[11]	24.0	1953
Pearse and Behrman[12]	20.6	1954
Mengert[13]	11.1	1954
Randall, J. H.[14]	27.4	1955
Henderson and Bean[15]	18.1	1957

In our series it is to be noted that if the granulosa-cell tumors are subtracted, the 5 year cure rate drops to 23.9 per cent for the remainder; if the pseudomucinous cystadenocarcinomas are further subtracted, the result becomes 20.3 per cent; if, finally, the serous papillary tumors classed as "borderline" in histology are subtracted, the 5 year cure rate drops to only 12 per cent. The conclusion must be that there was no improvement in the cure rate between the periods 1922-1943 and 1944-1951.

It was perhaps not to be expected that the absolute cure rate would rise very much, since the improvement in the therapy of ovarian cancer has occurred largely in the direction of a better planned radiation therapy, rather than in that of an extended surgical procedure. In general, postoperative x-ray therapy still has as its chief function a life-prolonging rather than a life-saving measure. Hence, improvement, if any has occurred, should be sought in the duration of survival rather than in absolute cure rates.

The effects of therapy in cancer of the ovary must, therefore, be studied not only in relation to 5 year cure rates, but also in relation to average number of months of life in the cases that end fatally. To examine possible changes in the latter relationship we have constructed a number of so-called "survival curves" in which the percentage is plotted of all patients originally treated who are still alive at successive 6 month periods after the original operation.

A. Histogenetic Type.—

The 5 year survival curve of different histogenetic types, as published in the 1949 report, is shown in Fig. 1. It portrays, in the rapid fall of the line, the high death rate during the first year, so that after 12 months a half of all patients have already died. Thereafter, losses are much slower and at the end of 60 months about 30 per cent of the followed patients are still alive. The curve for the serous papillary tumors follows rather closely that of the total group, probably for the mathematical reason that this is the most common type of tumor and contributes most substantially to the total figure. The survival curves for the granulosa-cell tumors and for the pseudomucinous tumors lie well above the average, perhaps because some actually benign tumors have been erroneously included in the group. Well below the average are the groups of cases designated as "undifferentiated" or "unclassified," groups which contain a high proportion of very advanced cases from which histological material was unavailable or too inadequate for accurate classification. From these latter groups no patient lived for 3 years.

In Figs. 1 and 2, the results for 1944-1951 are compared with those of the older cases. The chief conclusion is that the new cases have followed closely the pattern of the old. It will be noted that the relatively favorable types, the granulosa-cell tumors and the pseudomucinous cystadenocarcinomas, have done even better than in the earlier years and there have been no recurrences among the cases of pseudomucinous adenocarcinoma after the first year and none among the granulosa-cell tumors after the thirtieth month. The survival curve for all cases as well as for the serous cystadenocarcinomas, with its steep fall in the first 18 months and its gradual decline thereafter, and its 30 per cent of survivors at 5 years, remains substantially unchanged. The survival of one patient in the undifferentiated group is possibly to be regarded as a tribute to improved radiation therapy.

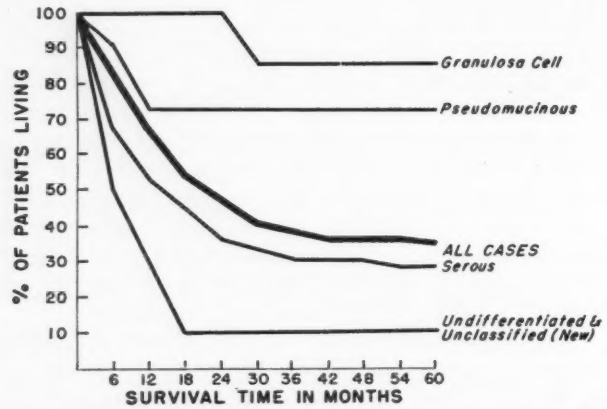


Fig. 1.—Five-year survival curves in carcinoma of the ovary according to histological type (new series, 1944-1951).

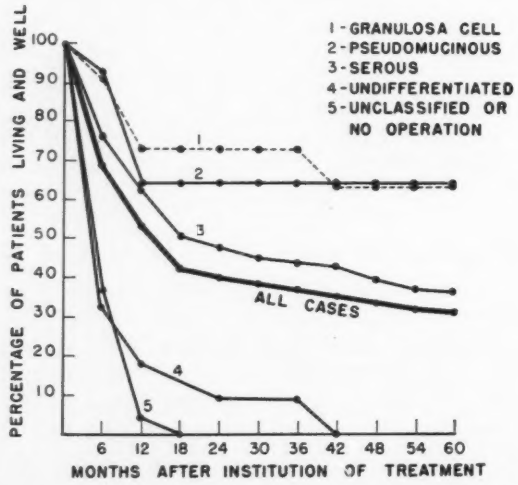


Fig. 2.—Five-year survival curves in carcinoma of the ovary according to histological type (old series, 1922-1943). (From Munnell and Taylor: Am. J. Obst. & Gynec. 58: 943, 1949.)

B. Histological Grade.—

The histological degree of malignancy is important in determining prognosis as shown by Table IV, which summarizes end results in this new series

according to histological degree of malignancy in the papillary serous cystadenocarcinomas, for it is only in this latter group that there is a sufficient number of cases to afford statistical significance.

TABLE IV. FIVE-YEAR SURVIVALS IN 105 CASES OF PAPILLARY SEROUS CYSTADENOCARCINOMA ACCORDING TO HISTOLOGIC DEGREE OF MALIGNANCY, 1944 THROUGH 1951

	TOTAL CASES	LOST TO FOLLOW-UP		DETERMINATE REMAINDER A-B1	5 YEAR SURVIVORS	RELATIVE 5 YEAR SURVIVAL RATE (%)	ABSOLUTE 5 YEAR SURVIVAL RATE (%)
		B1 WELL WHEN LOST	B2 PROBABLY DEAD				
Borderline	9	1	0	8	8	100	89
Grade I	10	0	0	10	5*	50	50
Grade II	36	2	2	34	7*	20.5	19.4
Grade III	50	1	1	49	5*	10.2	10.0
Total	105	4	3	101	25	24.7	23.8

*Three patients (1 from each group) died of recurrence *after* 5 years.

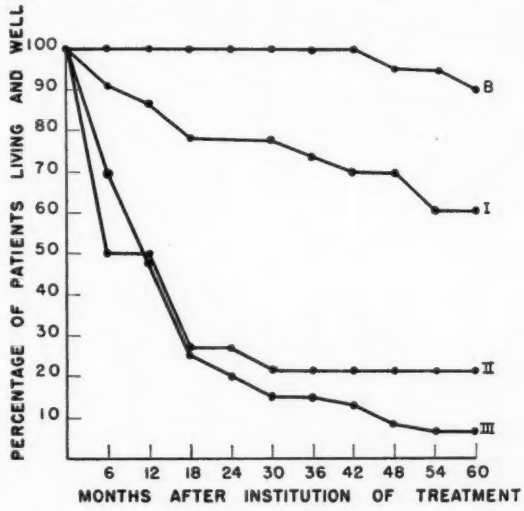


Fig. 3.—Five-year survival curves in papillary serous cystadenocarcinoma of ovary according to histological degree of malignancy (old series, 1922-1943). (From Munnell and Taylor: AM. J. OBST. & GYNEC. 58: 943, 1949.)

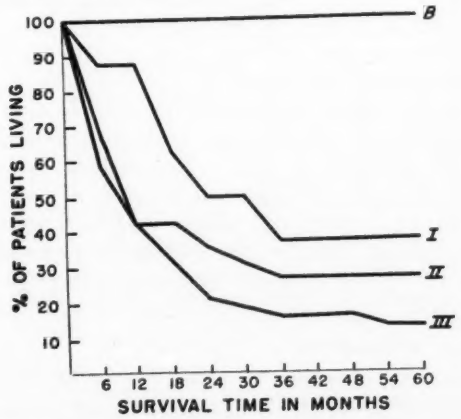


Fig. 4.—Five-year survival curves in papillary serous cystadenocarcinoma of ovary according to histological degree of malignancy (new series, 1944-1951).

The figure of the 1949 report (Fig. 3) showed this relationship rather clearly. Here it is evident that not only the 5 year cure rate but also the length of life of the patients who succumb to the disease is dependent upon the histological structure of the tumor present.

The new cases of 1944-1951, shown in Fig. 4, exhibit the same trends. In the new series there were no recurrences among the cases classed as "borderline." The Grade I cases in the recent series did not do quite as well as did the same cases in the earlier group, this perhaps being an artifact dependent upon unconscious and subjective differences in the manner of grading. The cases in Grades II and III did somewhat better in the recent series, possibly because of improvements in postoperative x-ray therapy, but the improvement is of course too small to be considered significant.

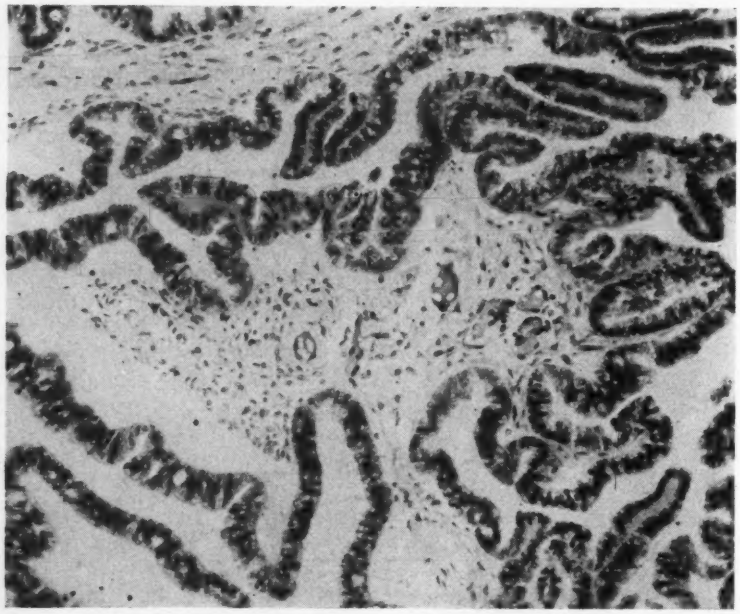


Fig. 5.—Photomicrograph of papillary serous cystadenocarcinoma of ovary, borderline.

A word must be said at this point about the justification for including the "borderline" group in a series of carcinomas at all, since in the recent series there were no recurrences. In the first place, let it be said that this group must not be used simply to improve an end result figure, and for this reason the figure with these cases excluded has also been clearly stated. Second, it can be shown that these tumors can and do sometimes recur and prove fatal to the patient. An example is that of a patient operated upon in 1935, who some 20 years later developed signs of pulmonary disease, and at whose autopsy multiple pulmonary metastases were observed with a histology of the type that we have designated "borderline" (Fig. 5). It is difficult not to regard as cancer a tumor of which even a rare example may have a course such as this one.

C. Clinical Extent of Disease.—

Table V summarizes end results in the new series according to clinical extent of disease and shows a clear-cut indication of poor prognosis once the disease has spread beyond one ovary. This is only slightly different from our

TABLE V. FIVE-YEAR END RESULTS IN 148 CASES OF CARCINOMA OF OVARY ACCORDING TO CLINICAL EXTENT OF DISEASE (NEW SERIES, 1944-1951)

	A	B		C	D	D/C	D/A
		LOST TO FOLLOW-UP					
STAGE	TOTAL CASES	B1 WELL WHEN LOST	PROBABLY DEAD	DETERMINATE REMAINDER A-B1	5 YEAR SURVIVORS	RELATIVE 5 YEAR SURVIVAL RATE (%)	ABSOLUTE 5 YEAR SURVIVAL RATE (%)
I	56	11	0	45	35	77.7	62.5
II	11	0	1	11	3	27.0	27.0
III	25	1	4	24	3	12.5	12.0
IV	56	3	6	53	1	1.8	1.7

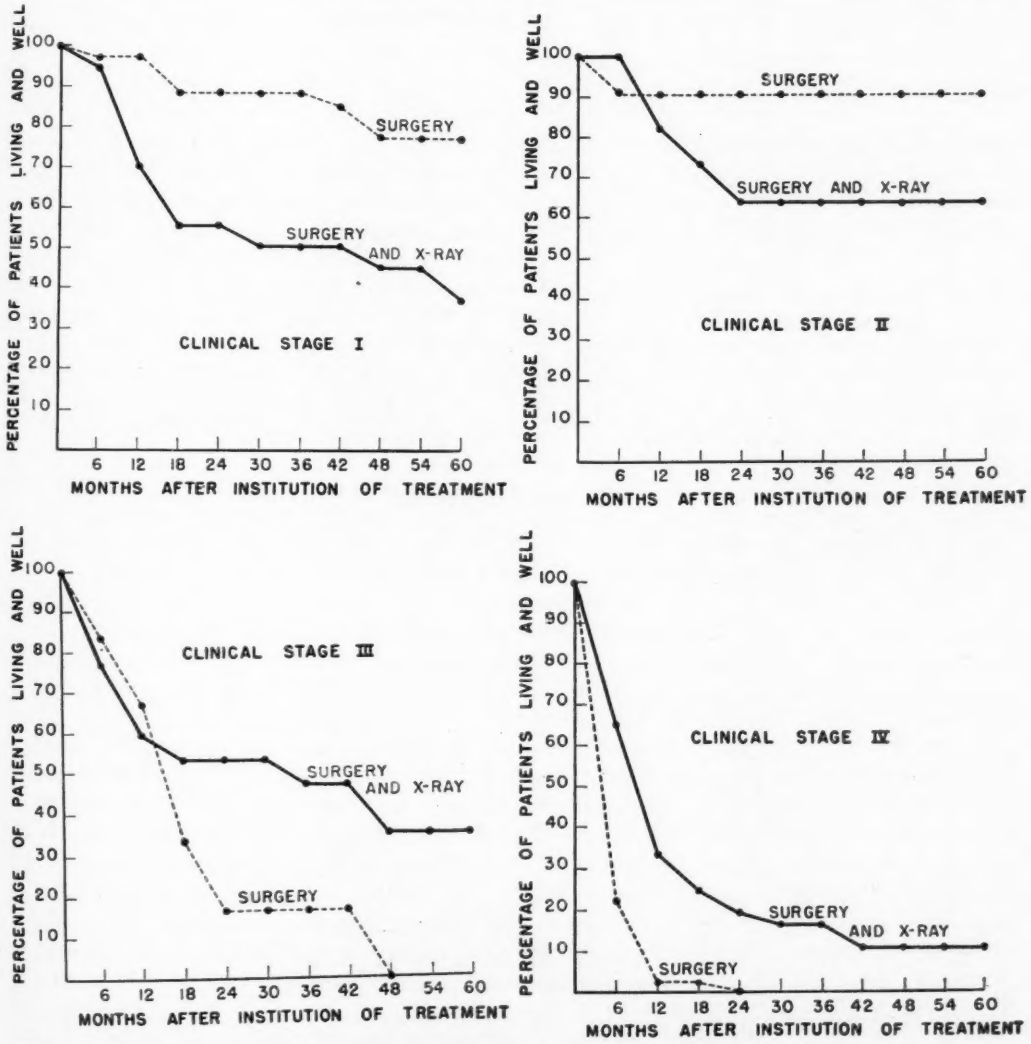


Fig. 6.—Five-year survival curves—clinical extent of disease and method of treatment (old series 1922-1943). (From Munnell and Taylor: AM. J. OBST. & GYNEC. 58: 943, 1949.)

1949 report in which the 5 year cure rates for the different clinical stages were as follows: Stage I, 59 per cent; Stage II, 80 per cent; Stage III, 20 per cent; Stage IV, 5 per cent.

Our 1949 results demonstrated the value of postoperative x-ray therapy in prolonging survival time in the more advanced cases, clinical Stages III and IV (Fig. 6). This same advantage is evident in the new series as shown in Figs. 7 and 8 in which one sees that in Stage III cases there were no survivors after 42 months unless postoperative x-ray therapy had been given, and no survivors after 18 months in the Stage IV cases unless x-ray therapy had been administered.

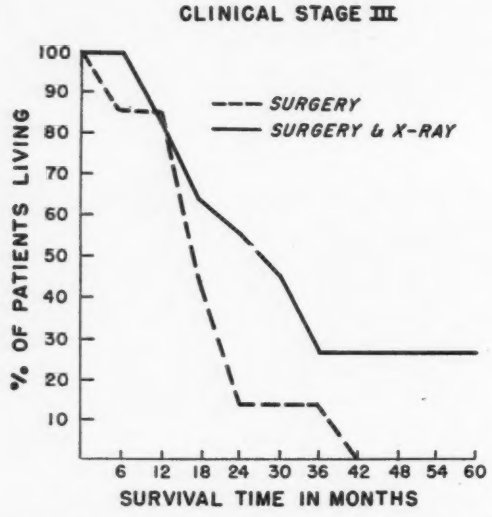


Fig. 7.—Five-year survival curves—clinical extent of disease and method of treatment—Stage III cancer of ovary (new series, 1944-1951).

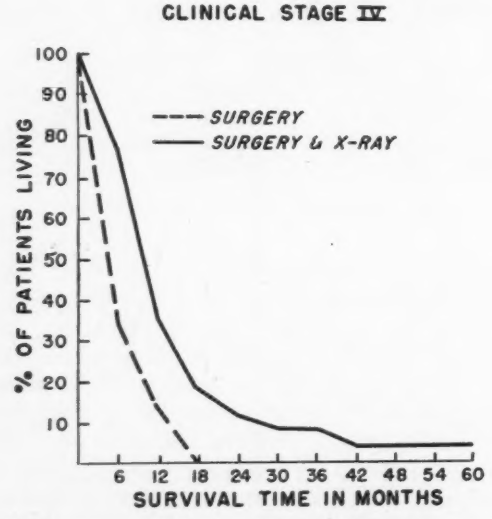


Fig. 8.—Five-year survival curves—clinical extent of disease and method of treatment—Stage IV cancer of ovary (new series, 1944-1951).

D. Spill at Time of Operation.—

A review of the cases in clinical Stages I and II, i.e., those in which the disease was limited to one or both ovaries, discloses the fact that spill at time of operation carries with it no apparently greater risk to the patient. Spill of the contents of the cyst took place at operation in 16 patients in this group,

12 of whom survived 5 years or longer, 5 receiving postoperative x-ray therapy, and 7 receiving none. These were all tumors of different histogenetic types and histological degrees of malignancy.

III. Newer Developments in Therapy

After reporting such little progress up to 1951, it is well for us to discuss what the present and immediate future may have to offer. Reference must therefore be made to the possibilities of prophylaxis, early diagnosis, better surgery, chemotherapy, and improved radiation treatment.

1. Prophylaxis.—The argument as to when to remove the apparently normal ovaries at the time of hysterectomy for benign pelvic disease goes on and there can be no satisfactory answer. Randall[16] has estimated that in only 3 patients in each 1,000 in whom ovaries are allowed to remain does ovarian cancer eventually develop. This datum provides a solid basis upon which to argue, but hardly offers an answer to the question.

2. Early Diagnosis.—The repeated routine gynecological examination has offered a possibility of detecting some early cases of ovarian cancer, but there are doubtless many gynecologists who in a lifetime have never found such a case. Javert[11] has estimated that a symptomless ovarian cancer will be found only once in 10,000 pelvic examinations.

Perhaps more stress should be placed on the importance of immediate examination of the patient with unexplained pelvic symptoms and the correct management of pelvic masses of undetermined nature. More can probably be accomplished so far as carcinoma of the ovary is concerned by the elimination of mistakes than by the multiplication of examinations in symptomless women.

3. Surgery.—The surgery of cancer of the ovary was standardized many years ago and little change that might be significant seems feasible. Total hysterectomy with bilateral salpingo-oophorectomy is standard procedure when possible. Exenteration operations, even by the most enthusiastic, are not advocated because of the known manner of dissemination of this type of cancer.

The possibilities of palliation, however, and even rarely of cure, impose real responsibility upon the surgeon to remove as much of the primary tumor and of omental masses as possible. The most valid criticism of current surgery for ovarian cancer seems to be the tendency of some operators to "open and close" only, to avoid the arduous and perhaps hazardous task of excising partly fixed carcinomatous masses from the pelvis, and the bulk of the omental metastasis. The removal of such masses certainly adds to the patients' immediate comfort and probably to the effectiveness of radiation therapy.

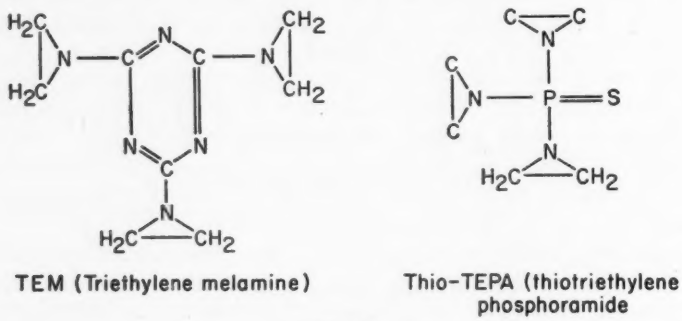
4. Chemotherapy.—The hopes for benefits from the chemotherapy of cancer, except in the instance of leukemia and the lymphomas, have certainly run far ahead of the demonstrable results. Among gynecological neoplasms, the ovarian carcinomas alone have provided some encouragement in this respect. For these, nitrogen mustard and its derivatives, triethylenemelamine (TEM) and thiotriethylene phosphoramide (thio-TEPA), have resulted in instances of real or fancied improvement (Fig. 9).

Triethylene-melamine (TEM) was one of the first compounds tried in ovarian carcinoma. In 1952 a report[22] appeared on the favorable response of 3 out of 4 cases of adenocarcinoma of the ovary, and more recently there has been a similar report[17] of a beneficial effect in 8 out of 26 cases. At the Francis Delafield Hospital such improvement seemed to occur in 3 out of 10 cases so treated.[18]

The other compound, thiotriethylene phosphoramide (thio-TEPA), has become available more recently. It, like nitrogen mustard (HN_2) and TEM, produces effects on cells somewhat similar to those of radiation, such as the inhibition of mitosis and the production of chromosomal abnormalities. Bateman,[19] as well as Shay and Sun,[20] has reported encouraging temporary improvement in advanced carcinoma of the ovary with the use of thio-TEPA.

At the Francis Delafield Hospital, in cooperation with the Department of Medicine, 27 patients with advanced carcinoma of the ovary have received treatment with thio-TEPA. The carcinoma in most of the cases was very extensive and the majority of the patients had already received maximum amounts of radiation therapy.

The thio-TEPA is administered intravenously in amounts usually of 20 mg. per injection, the usual course consisting of three injections given within one or two weeks. Therapy is then discontinued until the leukocyte and platelet counts return to normal, when the same or a smaller series of injections may be given. Great care must be taken both in initiating treatment and in repeating a course of injections because of the serious leukopenia and thrombocytopenia which may be produced.



TEM (Triethylene melamine) Thio-TEPA (thiotriethylene phosphoramide

Fig. 9.

Evaluation of treatment is difficult and must depend upon disappearance of ascites or pleural effusion, or the diminution in size of an abdominal mass. Based on these criteria, there was believed to have been objective improvement in 14 of the 27 cases treated. In addition to these objective signs, striking though fleeting subjective improvement seems to occur in a number of patients.[18]

While the practical value of this drug is certainly limited, it seems to have been demonstrated that it has at least merited a trial in the inoperable, advanced cases. That it may properly be given as a substitute for or preceding x-ray therapy has not been determined.

5. Radiation Therapy.—Much may be expected from the persistent, precise, and painstaking application of x-ray therapy in maximum tolerable doses, and in precise reference to the distribution of the disease.

Irradiation should be started as soon as the postoperative condition permits, usually within one to two weeks. In our departments, patients are being treated in the Presbyterian Hospital with 250 kv. and the betatron, and in the Francis Delafield Hospital with 2,000 kv. (Table VI). Conventional deep x-ray therapy to the lower abdomen and pelvis should aim to administer 3,500-4,000 r to the midpelvis in 3 or 4 weeks. Usually, two anterior and two posterior 10 by 15, 10 by 20, or 15 by 15 cm. ports are given a total of 2,000-2,400 r (in air) using 200-250 kv. and 1.0 to 1.6 mm. Cu half-value layer. It is important to include the entire wound in the field because of

the chance of implantation of neoplasm. If the entire abdomen must be treated, a total of eight portals, including four anterior and four posterior quadrants, are treated, an upper and a lower quadrant on the same side daily in rotation.

TABLE VI. X-RAY THERAPY OF CARCINOMA OF OVARY

With 250 kv. X-rays.—	
Constant factors	50 cm. target skin distance 2 mm. Cu filter
Pelvis only	Total tissue dose: 3,500-4,000 r Daily dose: 200 r in air to each of 2 anterior 10 by 15, 10 by 20, or 15 by 15 cm. fields alternating with opposing posterior fields
Entire abdomen	Total dose: 2,000-3,500 r Daily dose: 150-200 r in air to each of 2 anterior upper and lower fields, alternating with 2 parallel anterior upper and lower fields with 4 opposing posterior fields
With 2,000 kv. X-rays.—	
Constant factors	100 cm. target skin distance 7 mm. lead filtration
Pelvis only	Total tissue dose: 4,500-5,000 r Daily dose: 200 r total through opposing anterior and posterior fields, 15 by 15 cm.
Entire abdomen	Total dose: 3,500-4,000 r Daily dose: 100 r to each of two pairs of opposing fields

The same advantages and limitations of the use of the 24 million volt x-rays produced by the betatron apply as with 250 and 2,000 kv., namely, that it is a local form of treatment for increasing dosage, but it will not make a radioresistant tumor more sensitive.

It is doubtful that the response of the tumor is specifically related to x-ray wave length, but it is clear that with the higher voltages the skin effect will be relatively less in comparison with the required depth dose, a consideration of special importance for the previously irradiated and for the obese patient.

The plan in our Department is to irradiate only the lower abdomen in patients in whom no cancer nodules have been observed above the umbilicus at the time of operation. This decision was reached because it was believed that the larger dose which may be given when only half of the abdomen is treated is more desirable than the prophylactic coverage with a smaller dose of all the theoretically possible area of dissemination. In Stage IV, however, where tumor tissue has been observed in the omentum and other areas, the patient must accept the hardships of irradiation of the whole abdomen and the therapist a smaller dose for each unit volume of tissue treated.

With regard to radiation therapy, one should perhaps refer to the disappointment of the last 5 years. When radioactive colloidal gold, Au^{198}, first became available, the idea that a source of radioactivity could be injected into the peritoneal cavity in a fluid medium, which would cover every square centimeter of peritoneal surface was extremely attractive.

Probably because of the relatively slight penetrating power of the radioactivity of Au^{198} it was predicted that only the most superficial lesions would be affected. This has proved true and our experience has indicated that its only value is in the prevention of or delay in the accumulation of ascitic fluid.[21] Other reported experience has been similar.[14] There remains the theoretical possibility that Au^{198} instilled at or immediately after a surgical

operation in which the tumor appeared grossly to have been completely extirpated would prevent the implantation on the peritoneum of free-floating cancer cells or of microscopic aggregations of cells spread about as a result of the surgical procedure. The statistical proof of the value of such a prophylactic use of radiogold has promised to be so difficult as to have discouraged any serious attempt to set up a planned clinical study.

Summary

1. The results of the treatment of 148 cases of cancer of the ovary, from 1944 to 1951, inclusive, have been reviewed and compared with the results in cases treated from 1924 to 1943.

2. The importance of histogenetic type, histological grade, and stage of clincal extension in prognosis has again been stressed.

3. No significant improvement in the results in the more recent as compared with the earlier period was noted.

4. The prospect of successful chemotherapy and of improved x-ray therapy is discussed.

References

1. Randall, C. L., and Gerhardt, P.: Am. J. Obst. & Gynec. **68**: 1378, 1954.
2. Munnell, E. W.: Cancer **5**: 1128, 1952.
3. Munnell, E. W., and Taylor, H. C., Jr.: Am. J. Obst. & Gynec. **58**: 943, 1949.
4. Henderson, D. N.: Am. J. Obst. & Gynec. **62**: 816, 1951.
5. Flick, F. H., and Banfield, R. S.: Bull. Sloane Hosp. Women **2**: 31, 1956.
6. Allan, M. S., and Hertig, A. T.: Am. J. Obst. & Gynec. **58**: 640, 1949.
7. Schmitz, H. E., and Majewski, J. T.: Radiology **57**: 820, 1951.
8. Wheelock, F. C., Fennell, R. H., Jr., and Meigs, J. V.: New England J. Med. **245**: 447, 1951.
9. Kerr, H. D., and Elkins, H. B.: Am. J. Roentgenol. **66**: 184, 1951.
10. Randall, C. N., and Hall, D. W.: Am. J. Obst. & Gynec. **63**: 497, 1952.
11. Javert, C. T., and Roscoe, R. R.: S. Clin. North America **33**: 557, 1953.
12. Pearse, W. H., and Behrman, S. J.: Obst. & Gynec. **3**: 32, 1954.
13. Mengert, W. F.: South. M. J. **47**: 918, 1954.
14. Randall, J. H.: Obst. & Gynec. **5**: 445, 1955.
15. Henderson, D. N., and Bean, J. L.: Am. J. Obst. & Gynec. **73**: 657, 1957.
16. Randall, C. L.: Obst. & Gynec. **3**: 493, 1954.
17. Sykes, M. P., Rundles, R. W., Pierce, V. K., and Karnofsky, D. A.: Surg., Gynec. & Obst. **101**: 133, 1955.
18. Naujoks, H., Crandall, C., Tretter, W., and Gellhorn, A.: (In press.)
19. Bateman, J. C.: New England J. Med. **252**: 879, 1955.
20. Shay, H., and Sun, D. C. H.: Cancer **8**: 498, 1953.
21. Kligerman, M. M., and Habif, D. V.: Am. J. Roentgenol. **74**: 651, 1955.
22. Rundles, R. W., and Barton, W. B.: Blood **7**: 483, 1952.

THE STEIN-LEVENTHAL SYNDROME*

A Review and Case Reports

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IN 1935, Stein and Leventhal[1] were the first to correlate bilateral polycystic ovaries with a definite clinical syndrome which consists of menstrual irregularity, especially amenorrhea, and a history of sterility, in association with bilateral polycystic ovaries.

Diagnosis

Menstrual irregularities and sterility are the most common complaints of the patient. The menarche occurs, as a rule, at the usual age. The menses may be normal and at regular intervals for a period of time before they become irregular, or they may occur at irregular intervals from the menarche. The irregularity is often followed by hypermenorrhea, later by oligomenorrhea, and finally by varying periods of amenorrhea of from 8 weeks to as long as 9 years. Hypermenorrhea may be severe enough to cause acute anemia and even shock. Sterility is usually primary, but may develop subsequent to a pregnancy. Hirsutism occurs in approximately one half of these women, and a male escutcheon is fairly common. Obesity is fairly frequent. Underdevelopment of the breasts is seen, but infrequently. Acne sometimes occurs.

Pelvic examination occasionally reveals hypertrophy of the clitoris and often hypoplasia of the uterus. The ovaries are often not palpable because of the obesity, and sometimes a masculine type of abdominal musculature. Bilateral and simultaneously enlarged polycystic ovaries are absolutely necessary for a diagnosis of the Stein-Leventhal syndrome. If palpable, these ovaries are noted to be from two to four times normal size, and are cystic, insensitive, and usually not prolapsed into the cul-de-sac. Inability to palpate the enlarged ovaries does not eliminate the possibility of their presence.

Stein and his co-workers[1-6] have utilized pneumoroentgenography in over 90 patients and have been quite successful in demonstrating the enlarged bilateral polycystic ovaries and hypoplasia of the uterus. Repeated endometrial biopsies usually show a proliferative pattern of endometrium indicating that these patients have anovulatory menstrual cycles, but it is not uncommon for a patient with this syndrome to ovulate once or twice a year and follow each ovulation with a normal menstrual period. Culdoscopy has been used rather extensively by Kelly and Rock,[7] and less extensively by Meaker[8] and Stein,[6] and has proved to be of considerable benefit in making a diagnosis in many patients with sterility.

Many endocrine studies have been performed on the blood and urine of patients with this syndrome.[9-14] Briefly, estrogens and the follicle-stimulating

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hormone are consistently within normal range; 17-ketosteroids are usually within normal range but may be slightly elevated. Pregnanediol excretion has been shown to be elevated in a small number of patients, but this has not been studied extensively.[9, 11] Luteinizing hormone cannot be accurately assayed at this time. This is unfortunate since it is thought that this hormone may play a leading role in the etiology of this syndrome.[10, 12]

Pathologic Findings

On gross examination the surface of the ovaries is smooth, glistening, and usually white. There may be small bluish areas over some of the larger cysts, which may be visible through the capsule. The cysts are not usually elevated above the surface of the ovary. The ovary does not show the usual wrinkling due to previous ovulation and scarring, since these patients ovulate only rarely. No freshly ruptured follicles or corpora lutea are seen. On cut section the thickened tunica albuginea shows up as a thick white layer. The stroma is usually dense and tough and there are multiple cysts ranging in size from a few millimeters to 1.5 cm. situated in the periphery of the ovary just beneath the capsule.

Microscopic examination of these ovaries reveals rather consistent findings. The tunica albuginea is usually noticeably thickened. It has been described as a "dense collagenous material made up of interlacing lamellae of connective tissue."[9] There are multiple follicle cysts, varying in size from a few millimeters to 1.5 cm., which are usually limited to the cortex of the ovary just beneath the tunica. Numerous follicles in all stages of development are seen. These cysts may be lined by a single layer of granulosa cells, but the more advanced ones are lined only by theca cells. The theca interna is usually hyperplastic and often shows luteinization. Occasionally a corpus albicans and rarely a corpus luteum may be seen. Fairly normal Graafian follicles may be seen which appear to be developing normally. The stroma is usually dense and fibrous.

Pathogenesis

The etiology of this condition remains obscure. It has been shown not to be congenital, inflammatory, or degenerative.[1-6] It has been suggested that there is a mechanical barrier which operates to prevent the immature Graafian follicles from ripening and reaching the surface.[1, 9, 15] The thickened tunica albuginea with the large number of cystic follicles crowded together in the ovarian cortex, which do not rupture on the surface of the ovary, is in favor of this theory. Further evidence is the restoration of physiologic function following the removal of the thickened tunica and cystic cortex of the ovary.[16] However, bilateral simultaneous enlargement of the ovaries seems to indicate that an extraovarian stimulus is the primary responsibility. Stein[3] has stated, "It is the result of a definite endocrine disorder." He has theorized that the anterior lobe of the pituitary is at fault and suggests the possibility of an early overproduction of follicle-stimulating hormone which causes a large number of Graafian follicles to grow simultaneously. When this continues over a long period of time, the follicles become cystic, crowded together, and cause a thickening of the tunica albuginea. Repeated determinations of the follicle-stimulating hormone, however, have been within normal range. This casts some doubt on the theory.[9] Haas and Riley[10] feel that the follicle development begins more or less normally, but that there is something lacking to complete the ovulatory process. The follicles then become atretic and the ovary becomes polycystic.

There is experimental evidence that progesterone inhibits ovulation by inhibiting production of luteinizing hormone by the pituitary.[11] Since pregnanediol excretion has been shown to be consistently elevated in a number of patients, Fischer and Riley[11] have concluded that the pregnanediol comes from an elevated progesterone level and feel that the failure of ovulation is induced by the suppression of luteinizing-hormone activity of the anterior pituitary.

Studies of the ovarian circulation have added light to the mechanism of formation of ovarian cysts. Reynolds,[17] studying the ovarian circulation in the rabbit, and Delson,[18] working with the human ovary, have demonstrated that the spiral nature of the arterioles is necessary for growth and accommodation when the ovary is stimulated by gonadotrophic hormones. They have shown that the blood pressure in the terminal arterioles is controlled by the spiraling, and the orderly change in pressure follows the normal growth and regression of the follicles. Normally, many follicles begin to mature with each cycle, but never rupture and later degenerate. It is possible that with a derangement of the normal endocrine mechanism, the atretic follicles may be stimulated and become larger than normal. According to Reynolds and Delson, there is a distortion of the spiral arterioles in the region of these cysts, and they become straightened. When the arterioles become straightened there is an increase in the blood pressure, which results in a transudation of fluid into the enlarged follicles. If this process is repeated frequently, the cortex of the ovary may become crowded with these enlarged follicles and produce a typical polycystic ovary.

Greenblatt[12] has suggested that the hyperthecosis, so frequently seen, may be the result of excess pituitary stimulation of the ovaries, probably by the luteinizing hormone.

Treatment

The most satisfactory treatment for the Stein-Leventhal syndrome appears to be wedge resection of the ovaries. The remaining follicle cysts are perforated and the defect is closed with fine catgut. Other techniques have been used with less strikingly beneficial results. Bailey[16] has recommended wedge resection of the ovaries with extroversion. Robinson,[19] Reycraft,[20] and Jacobson[21] have recommended decortication or stripping of the ovarian capsule. Others have used x-ray therapy[22] to the pituitary gland and ovaries, dilatation and curettage,[22] and various types of hormone therapy[1-6, 8-14] with poor results.

Stein,[6] Stern[23] and others[24, 25] have recommended that dilatation and currettage be performed on all patients with menometrorrhagia associated with this syndrome to rule out endometrial carcinoma.

Case Reports

CASE 1.—Mrs. A. W. C., gravida 0, aged 28 years, was first seen on Feb. 20, 1952, with a history of sterility for 5 years and varying periods of oligomenorrhea since the menarche. Previous sterility treatment was unsuccessful. She had marked hirsutism. Pelvic examination showed slight hypertrophy of the clitoris, the uterus was normal in size and anteflexed, and the right ovary was enlarged three to four times. Hormone therapy was unsuccessful. On Jan. 11, 1953, a dilatation and curettage, right oophorectomy, and wedge resection of the left ovary were done. Her first menstrual period occurred Feb. 7, 1953, and menses were regular every 28 to 30 days. She became pregnant and delivered a living child on Nov. 11, 1954. Since delivery her menstrual periods have remained regular every 28 to 30 days.

The right ovary was white, enlarged four to five times normal size, tough, with a thickened capsule, and polycystic. The left ovary was slightly enlarged but of the same appearance. The pathology findings (Figs. 1 and 2) were consistent with the Stein-Leventhal syndrome.

CASE 2.—Mrs. L. D. P., gravida 0, aged 23 years, was first seen on Sept. 11, 1954, with a history of sterility for 4½ years and irregular menses since the menarche at 14 years of age. She had episodes of amenorrhea and others of hypermenorrhea. A dilatation and curettage had been performed in January, 1954. Examination disclosed slight hirsutism, a small uterus, and both ovaries enlarged three to four times normal size. Hormone therapy was unsuccessful. On Sept. 29, 1954, a menstrual period started after 3 months of amenorrhea and she continued to bleed with occasional flooding. She was admitted to the hospital on Nov. 1, 1954, with profuse vaginal hemorrhage and shock. The hemoglobin was 5.75 grams and she was transfused with 2,000 c.c. of whole blood. A dilatation and curettage was done and the pathology diagnosis was cystic hyperplasia of the endometrium. On Nov. 9, 1954, a wedge resection of the ovaries was performed. Her first menstrual period was Dec. 7, 1954. She was delivered of a living child on Dec. 15, 1955. Since delivery her menstrual periods have occurred every 30 to 34 days.

The ovaries at operation were enlarged three times normal size with the typical gross appearance of the Stein-Leventhal syndrome. The pathology findings (Fig. 3) were consistent with the Stein-Leventhal syndrome.

This patient became pregnant for the second time, but had a spontaneous abortion on Feb. 11, 1957.

Fig. 1.

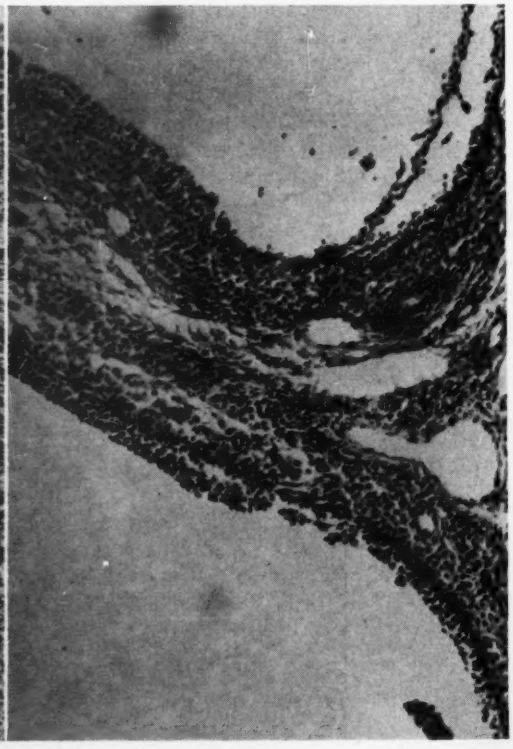

Fig. 2.

Fig. 1.—Shows thickened tunica albuginea.
Fig. 2.—Shows follicle cysts back to back.

CASE 3.—Mrs. T. E. E., gravida 0, aged 28 years, was first seen on June 2, 1953, with a history of sterility for 5½ years and amenorrhea. Her menarche occurred at 13 years of age and the intervals between her menstrual periods were 30 days to 5 months with oligomenorrhea. Examination showed slight hirsutism, a small cervix with stenosis, a small uterus, and ovaries of normal size. Hormone therapy was unsuccessful. On June 9, 1956,

she complained of having had no menses since July, 1955. Examination showed a definite male escutcheon, slight hypertrophy of the labia minora, and enlargement of both ovaries to twice normal size. X-ray of the skull disclosed a normal sella turcica. Papanicolaou smears showed no tumor cells. A hysterosalpingogram was normal. 17-ketosteroids were 10.5 mg. in 24 hours. A dilatation and curettage and wedge resection of the ovaries were done on June 22, 1956. Her first menstrual period was July 20, 1956. Menses have occurred every 27 to 29 days since the operation.

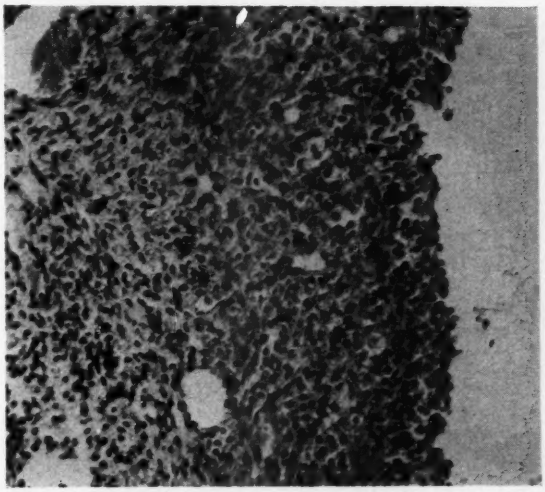

Fig. 3.—Shows luteinization of the theca interna.

Fig. 4.—Shows luteinization of the theca interna and flattened granulosa layer.

Both ovaries were enlarged two to three times normal size; had a thick, tough capsule; were cystic, and whitish gray. The pathology findings were consistent with the Stein-Leventhal syndrome.

She is now pregnant and her prenatal course is progressing satisfactorily.

CASE 4.—Mrs. H. L. W., gravida 0, aged 22 years, was first seen on May 13, 1955, with a history of sterility for 1½ years and amenorrhea. The menarche occurred at 11 years of age and the intervals between her menstrual periods were 28 days to 6 months. Pelvic examination showed a small cervix and uterus, and the right ovary enlarged two to three times. A Rubin test revealed patency of the Fallopian tubes. The basal metabolism rate was minus 5 per cent. She had profuse vaginal bleeding during November and December, 1955, and the left ovary was then noted to be slightly enlarged also. On Jan. 6, 1956, a dilatation and curettage was done. The pathologist reported a proliferative type of endometrium. In March, 1956, she again experienced profuse bleeding so another dilatation and curettage was performed. This also revealed proliferative-type endometrium. The hemoglobin was 7.5 Gm. and she was transfused with 1,000 c.c. of whole blood. In June, 1956, she had another episode of profuse hemorrhage, and on June 29, 1956, a uterine curettage and wedge resection of the ovaries were done. Her first menstrual period was Aug. 2, 1956. Menses have occurred every 29 to 32 days since the last operation.

Both ovaries were twice normal size, cystic, white, and had a thickened capsule. The pathology findings were consistent with the Stein-Leventhal syndrome.

CASE 5.—Mrs. F. R. F., gravida i, abortion i, aged 23 years, was first seen on March 30, 1951, with a history of secondary sterility of one year's duration and periods of irregular menses with oligomenorrhea. The menarche occurred at 12 years of age with menstrual periods at intervals of 31 days to 6 months. Examination showed slight hirsutism, a small uterus, and no detectable enlargement of the ovaries. On April 5, 1951, she complained of vaginal spotting which became progressively worse and on April 14, 1951, a dilatation and curettage and biopsy of the cervix were done. The pathology reports showed a proliferative type of endometrium and chronic cervicitis. Periods of amenorrhea continued, and on Dec. 4, 1951, both ovaries were slightly enlarged. Hormone therapy was unsuccessful. On Sept. 4, 1956, a dilatation and curettage and wedge resection of both ovaries were done. Her first menstrual period was Oct. 15, 1956.

The ovaries were two to three times normal size, white, and had a tough and thickened capsule. The pathology findings (Fig. 4) were consistent with the Stein-Leventhal syndrome.

Results and Comment

In our small series of 5 cases, the most common complaints have been sterility of one to 5½ years' duration and amenorrhea varying from 3 to 11 months' duration. Four of the 5 patients had hirsutism of varying degrees. All 5 of the patients had bilaterally enlarged polycystic ovaries ranging from two to five times normal size.

Two patients experienced hypermenorrhea severe enough to necessitate transfusions of whole blood to correct the anemia from blood loss. A dilatation and curettage was necessary to control the hemorrhage in each case. One patient suffered profound shock from hemorrhage.

Two of the 5 patients have become pregnant and delivered normal, living children. The other 3 patients have not been followed for a sufficient period of time to establish their fertility. The husbands of all the patients were checked for fertility prior to any operative procedure.

All 5 patients resumed a normal menstrual pattern within 5 weeks subsequent to bilateral wedge resection of the ovaries. A dilatation and curettage was done on all patients in this series. The gross and microscopic pathology findings in each case were consistent with those of the Stein-Leventhal syndrome.

The results obtained from surgical treatment of this syndrome have varied. Stein and his co-workers have treated 90 cases successfully. Eighty-nine per cent of 64 infertile patients became pregnant, a total of one hundred and twenty

times. There were no failures and no recurrences. Auer,[26] however, has reported one case of proved recurrence. Bailey[16] reported upon 17 patients operated upon, 13 of whom developed regular menses afterward. Only one of his patients became pregnant, but the others had not been followed for a sufficient period of time. Klinefelter and Jones[27] reported that 90 per cent of their patients resumed normal menstrual function. Sixty-five per cent became pregnant. Meaker[8] reported that 77 per cent of his patients with menstrual irregularity and amenorrhea were relieved, and 66 per cent of his infertile patients conceived. Ingersoll and McDermott[9] reported satisfactory results in 68 per cent of their patients.

Following wedge resection of the ovaries in the treatment of this syndrome, hypoplasia of the uterus and underdevelopment of the breasts are usually corrected in a short period of time.[6] The patient's mental attitude usually improves markedly. Obesity and acne, when present, usually improve immediately. The patient's menstrual periods usually are resumed within five weeks following operation and as a rule remain regular. Pregnancy usually occurs within an average of 5 months. If pregnancy does not occur within a reasonably short period of time, however, the likelihood of conception is remote. The hirsutism persists, although there are a few reports[12, 28] to indicate that it may improve somewhat following operation.

Summary

A review of the literature has been presented.

Five cases of the Stein-Leventhal syndrome have been presented.

We wish to express our deep appreciation to Dr. Saul Kay, Medical College of Virginia, Richmond, Virginia, for reviewing the tissue section slides and to Dr. Julien H. Meyer, Roanoke, Virginia, for permission to use 2 of his cases.

References

1. Stein, I. F., and Leventhal, M. L.: Am. J. Obst. & Gynec. **29**: 181, 1935.
2. Stein, I. F., and Cohen, M. R.: Am. J. Obst. & Gynec. **38**: 465, 1939.
3. Stein, I. F.: Am. J. Obst. & Gynec. **50**: 385, 1945.
4. Stein, I. F., Cohen, M. R., and Elson, R.: Am. J. Obst. & Gynec. **58**: 267, 1949.
5. Leventhal, M. L., and Cohen, M. R.: Am. J. Obst. & Gynec. **61**: 1034, 1951.
6. Stein, I. F.: West. J. Surg. **63**: 319, 1955.
7. Kelly, J. V., and Rock, J.: Am. J. Obst. & Gynec. **72**: 523, 1956.
8. Meaker, S. R.: Fertil. & Steril. **1**: 293, 1950.
9. Ingersoll, F. M., and McDermott, W. V.: Am. J. Obst. & Gynec. **60**: 117, 1950.
10. Haas, R. L., and Riley, G. M.: Obst & Gynec. **5**: 657, 1955.
11. Fischer, R. H., and Riley, C. L.: J. Clin. Endocrinol. **12**: 890, 1952.
12. Greenblatt, R. B.: Am. J. Obst. & Gynec. **66**: 700, 1953.
13. Andrews, M. C.: Virginia M. Monthly **79**: 544, 1952.
14. Siegler, A. M.: Am. J. Obst. & Gynec. **64**: 431, 1952.
15. Dutoit, D. A. H.: Polycystic Ovaries, Menstrual Disturbances, and Hirsutism, Leyden. Holland, 1951, Stenfort Kroese. (Referred to by Haas and Riley.[10])
16. Bailey, K. V.: J. Obst. & Gynaec. Brit. Emp. **44**: 637, 1937.
17. Reynolds, S. R. M.: Endocrinology **40**: 381, 1947.
18. Delson, B.: Am. J. Obst. & Gynec. **57**: 1120, 1949.
19. Robinson, M. R.: Am. J. Obst. & Gynec. **30**: 18, 1935.
20. Reycraft, J. L.: Am. J. Obst. & Gynec. **35**: 505, 1938.
21. Jacobson, P.: Surg., Gynec. & Obst. **87**: 31, 1948.
22. Siegler, S. L.: Fertility in Women, Philadelphia, 1944, J. B. Lippincott Company, pp. 357-359.
23. Stern, O. N.: Delaware M. J. **28**: 29, 1956.
24. Dockerty, M. B., Lovelady, S. B., and Foust, G. T., Jr.: Am. J. Obst. & Gynec. **61**: 966, 1951.
25. DeVere, R. D., and Dempster, K. R.: J. Obst. & Gynaec. Brit. Emp. **60**: 865, 1953.
26. Auer, E. S.: Discussion of Leventhal and Cohen.[5]

27. Klinefelter, H. F., and Jones, G. E. S.: J. Clin. Endocrinol. 14: 1247, 1954.
28. Fraenkel, L.: J. Clin. Endocrinol. 3: 557, 1943.

Discussion

DR. CURTIS G. REBECK, Tampa, Fla.—As has been brought out by Drs. Ellett and Barnes, the etiology of this disorder is obscure. It is apparently an acquired disorder, and probably associated with a disturbance in the pituitary-ovarian relationship. The pathology found seems to indicate prolonged unopposed follicle-stimulating hormone action upon the ovary, not necessarily excessive blood levels of follicle-stimulating hormone, and an inability of the follicles to react to luteinizing hormone. If we look for a group of women with ovaries exposed to prolonged action of the follicle-stimulating hormone, we would find most of them in their early menstrual life, as we think of the first cycles after the onset of the menses as anovulatory. Perhaps in these individuals the anovulatory cycles continue until the changes in the ovary become irreversible, and the ovary fails as a receptive end organ to normal pituitary stimulation. It is in this group of women in early menstrual life that the Stein-Leventhal ovaries must develop. Certainly, the 5 patients cited by Dr. Ellett and Dr. Barnes all had atypical periods suggesting anovulatory cycles, starting from the onset of menses.

A recent report is interesting in pointing out the high incidence of endometrial carcinoma in women who were found to have bilateral polycystic ovaries. For those who feel that prolonged estrogen stimulation of the endometrium is associated with endometrial carcinoma, this correlation between the Stein-Leventhal syndrome and fundal carcinoma should be a welcome report. It also seems that the diagnosis of the Stein-Leventhal syndrome indicates continued follow-up of these patients through later life. It is of interest, but of questionable significance, that in the cases reported today the basal metabolic rate was elevated very slightly above normal in 2 instances, and was within normal limits in 3. This is in keeping with other reports. The empiric use of thyroid in menstrual irregularities has long been made by gynecologists with some claim to success. I wonder if any of Dr. Ellett's patients received thyroid therapy for any length of time prior to operation. Since most of these women present themselves as having sterility problems, I would be interested in how much of a sterility work-up was done on these patients prior to the decision to operate.

DR. WILLIAM E. BYRD, Norfolk, Va.—From our office files there have been 5 patients with this disease who have undergone laparotomy. The results were as follows:

One patient had regular menses for 2 years and then reverted to an amenorrheic pattern without an intervening pregnancy.

The second never had a sterility problem, the laparotomy being advised on the basis of pain and enlargement of the ovaries. She had 2 full-term pregnancies prior to and one subsequent to wedge resection.

The third resumed regular menses and has continued so for 18 months following operation. There have been no pregnancies, however.

The fourth patient has been symptomatically relieved of pelvic pain and partially regulated in her cycle but without pregnancy for a period of 12 months.

The last patient became regular in her menses for 8 months and then resumed an amenorrheic pattern which has continued for over 2 years. She is at present in the divorce court because of domestic difficulties secondary to her childlessness.

In brief, therefore, wedge resection in my hands has not been as successful in correcting the primary indication for laparotomy, namely, infertility, as it is in the hands of others.

We have in our office files 6 other patients with a clinical diagnosis of the Stein-Leventhal syndrome but who have not been operated upon. The clinical picture in these patients remains essentially unchanged. It is apparent that in our office the only indications for laparotomy and wedge resection are and have been infertility and pain associated with enlargement of the ovaries.

The recent article of Jackson and Dockerty showing a high incidence of endometrial carcinoma suggests that our method of management may not be without some risk as these patients approach menopausal age. However, for the present we will continue the conservative management and await further evidence.

DR. JAMES L. REYCRAFT, Cleveland, Ohio.—We have been intensely interested in this problem for some time. In 1937, I reported 7 cases in which a study along these lines was made, and treatment by cortectomy was carried out. That was before the Stein-Leventhal syndrome was as well recognized as it is today. In the course of time, we began thinking of the ovaries as sclerocystic, and were interested in them as such.

I have emphasized, and I think justly, that it is not necessary to do a culdoscopy or pneumoperitoneal study to diagnose these cystic ovaries. It is to me primarily a case of endocrine imbalance in which many follicles never rupture, and the tunica becomes very thick. You can palpate these ovaries bimanually and tell their character by their consistency, and combine your findings with the clinical symptoms.

In the second group of 11 cases which I reported in 1947, there was one case of theca-cell tumor, and one of Chiari's syndrome, but the remaining 9 cases were typical.

In the past 10 years, I have had the opportunity of performing 9 more operations for sclerocystic ovaries. If we do 7 in 10 years, then 11 in the next 10, and 9 in a third 10 year period, it must indicate to you that we have not abused the subject. Dr. Ellett's warning to be conservative about surgery in this field is well taken.

The so-called cortectomy consists of excising part of the cortex, and controlling bleeding with mattress sutures of No. 3-0 plain catgut. In the past several cases, we have sewn a patch of Gelfoam over the denuded area, and thereby the bleeding is well controlled.

Seven of the 9 patients in our recent series have had at least one child since the operation.

DR. ELLETT (Closing).— Dr. Rorebeck asked if any of these patients had been on thyroid therapy prior to the operation. Each one of the patients had been studied for a fairly long period of time. The first patient was studied for sterility for 5 years before we saw her and we followed her for a period of 11 months prior to operation. When she came into the office she was taking 3 grains of thyroid a day that a previous doctor had given her. We, of course, obtained a metabolism test. We frequently, in sterility problems, give thyroid, ½ grain daily, regardless of normal results of a basal metabolism test. The second patient had a sterility problem for 4½ years prior to seeing us. In the first 1½ months that she was under our care, she was admitted to the hospital for profuse vaginal bleeding complicated by shock and she was given 2,000 c.c. of whole blood. A curettage was done and the pathology report revealed cystic hyperplasia of the endometrium. About a week later we performed a wedge resection of the ovaries bilaterally and she has been well ever since that time. She has had one child and is now pregnant again. Case 3 had a total of 8½ years of sterility work-up. We worked with her for 3 years prior to operation. The fourth patient we saw for one year. She was admitted to the hospital on three different occasions for excessive vaginal bleeding. In one instance the hemoglobin was 7.5 Gm. and we transfused her with 1,000 c.c. of whole blood. On the third admission we did a third curettage and wedge resected the ovaries and her menstrual periods have resumed a normal pattern; however, she is not pregnant. Case 5 we saw personally for 5½ years prior to operation. She had become pregnant one time previously but aborted spontaneously between the fifth and sixth months. All of these patients received thyroid therapy prior to any operative procedure.

A FAMILY AFFAIR*

The Presidential Address

JOHN C. BURWELL, JR., M.D., GREENSBORO, N. C.

SINCE man's first appearance on earth the family unit has served as the cornerstone of a constantly developing social structure. Though permitted to serve for some time as guardian and adviser, only in the relatively recent past has the physician played any important role in family regulation. It is therefore perhaps fitting that we should pause to examine some of our opportunities and responsibilities in this field.

Matters of family expansion and family limitation rightfully belong in the province of the obstetrician-gynecologist. Yet, because we are frequently occupied with concerns more challenging to our professional skills, some of us are prone to neglect this duty in spite of its tremendous importance to the family. Let us consider for a few minutes the matter of family expansion.

Treatment of Sterility

Sterility studies are time consuming, financially unproductive, and the results frequently frustrating; but, when successful, rewarding beyond measure to both family and physician. Curiosity as to our own standing in the treatment of sterility prompted a statistical evaluation of the results in a two-man partnership over the 10 year period of January, 1946, to January, 1956. For the purposes of this discussion only successful studies are reported. Dr. Bertling and I included only those who had attempted pregnancy without contraceptives for a period of at least two years.

Since we are chiefly concerned with an obstetric practice, both our methods and results leave much to be desired. We do insist that the male partner cooperate at least to the extent of a Huhner test or preferably examination by a competent urologist. Extensive studies on the female partner are deferred until the husband has been declared of at least average fertility. The patient herself receives, with the aid of charts and extensive consultation, a detailed explanation of the processes of conception at the time of her initial visit. Results are never promised, but she is given the assurance that a careful and conscientious study will be made and that the possibility of success merits at least her full cooperation. A complete physical examination along with blood studies and urinalysis is recorded. Therapy is instituted when vaginitis, cervicitis, or lowered cervical pH is encountered. She is then sent home with basal temperature charts and daily dosages of vitamin E, the latter being given more for its psychic value than for any possible physiologic responses. Return visits are devoted to attempted correction of suspected or proved handicaps—progressing from such minor things as sperm nourishment to more complicated procedures such as salpingoplasty and irradiation of the pituitary. The latter were resorted to so infrequently as to be hardly worth the mentioning. Possible physical deterrents encountered are listed in Table I.

*Presented at the Nineteenth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Charleston, S. C., Feb. 6-9, 1957.

TABLE I. DEFECTS TO WHICH THE STERILITY MAY HAVE BEEN RELATED

Cervicitis	18
Endocrine dysfunction	15
Male subfertility	15
Vaginitis	12
Endometriosis	4
Cervical stenosis	3
Stein-Leventhal syndrome	3
Ovarian tumors	2
Cervical polyps	2
Tubal occlusion	1
Fibroid tumors	1
Chronic pelvic inflammatory disease	1
Congenital deformities	1
Total	78

Evaluation of 37 patients did not reveal any pathologic lesions which could be considered pertinent. Corrective measures instituted may or may not have had bearing on the outcome, but are listed in Table II.

TABLE II. MEASURES EMPLOYED FOR THE DIAGNOSIS AND THERAPY OF INFERTILITY PATIENTS

Basal temperature charts or fern test	93
Dietary vitamin supplements	64
Sperm nourishment with favorable vaginal pH	55
Basal metabolism tests and thyroid therapy	52
Dilatation and curettage	21
Cauterization of cervix	13
Local chemotherapy for vaginitis	12
Tubal insufflation or hysterosalpingography	12
Cyclic hormone therapy	10
Artificial insemination	5
Ovarian resection	3
Salpingoplasty	1
Irradiation of the pituitary	1

During this 10 year period, while under treatment, 115 women conceived and, of this number, 101 delivered normal living infants. Seventy-two of these were patients with primary sterility whose average time without contraceptives was 48 months, the longest being recorded as 12 years. There were 43 in the secondary sterility group, and their average time without contraceptives was 38 months, the longest time here being 7 years. For both groups the average time without contraceptives was 44 months.

In the primary sterility group the average length of treatment prior to conception was 14 months. Six patients required 4 years or longer, and one needed 7 years of consultation and treatment. Eight, or 11 per cent, conceived after one month of study, 20, or 27 per cent, conceived after 3 months, 25, or 34 per cent, conceived after 4 months, and 19, or 28 per cent, required from 5 months to 7 years, as shown in Table III.

TABLE III. DURATION OF TREATMENT PRIOR TO CONCEPTION IN PATIENTS WITH PRIMARY STERILITY

Longest period of study 7 years	
Average period of study 14 months	
After 1 month of study	11%
After 3 months or less	27%
After 4 months or less	34%
After 5 months to 7 years	28%

Table IV shows the average length of treatment in the secondary sterility group as 10 months, the longest as 4 years, with 4 patients needing 3 years or longer. Five, or 11 per cent, conceived after one month of study, 11, or 25 per cent, conceived after 3 months, 16, or 37 per cent after 4 months, and 11, or 27 per cent took from 5 months to 4 years. The totals for both groups vary so little that further tabulation is unnecessary, but one striking figure stands out so prominently as to demand careful attention. Forty-four, or 38 per cent of the 115, conceived within 3 months or less following their initial visit and 85, or 73 per cent, within 4 months or less.

TABLE IV. DURATION OF TREATMENT PRIOR TO CONCEPTION IN PATIENTS WITH SECONDARY STERILITY

Longest period of study 4 years	
Average period of study 10 months	
After 1 month of study	11%
After 3 months or less	25%
After 4 months or less	37%
After 5 months to 4 years	27%

It would require considerable elasticity of the imagination to conclude that active therapy played any great part in the successful outcome of this number in so short a period of study. Somewhere one of the psychic intangibles must be given its full share of credit. Dr. Lee Buxton, whose large series makes this one seem like the proverbial drop in the bucket, emphasizes the importance of patient reassurance as a form of psychic therapy. Certainly kindly interest coupled with a friendly understanding may accomplish as much as more spectacular scientific studies.

The outstanding feature of this series is, of course, that it represents an average sample of patients seen in an obstetrical practice. These figures will not vary greatly for the average obstetrician-gynecologist who does not make the treatment of sterility a specialty. Its very mediocrity should commend it to us for closer attention. Here are 101 individuals who might not have entered society without the expenditure of this time and effort on the part of the physician. If we may presume on probability to multiply this figure by 100 (or the ratio of the two physicians concerned with this series to the total membership of this organization) we arrive at the astonishing total of 10,000 new individuals. I wonder how many of us have realized that the members of this Association have played such a part in influencing our population during the past 10 years? If we may go a step further and again multiply this number by the ratio of certified obstetrician-gynecologists practicing in the United States, we reach the amazing figure of 200,000 new citizens.

When we consider that these new citizens, for the most part, come into homes where they are not only eagerly anticipated but where they are, as a rule, assured of proper educational advantages, their impact on the cultural and scientific future of the nation is as astounding as it is gratifying. Reflection on this accomplishment brings us to the conclusion that time spent in the interest of family expansion may be time indeed well spent. Just a little patience and a little understanding may be more productive than we can realize.

Family Limitation

Let us turn for a few moments to a consideration of the opposite side of the problem—that of family limitation. This phase of our family responsibility has received a great deal of attention from many sources, and its varied

aspects have been emphasized by a number of our own members—particularly by Dr. Frank Lock and Dr. John Cotton Tayloe. For some of us it is not a problem, since the idea is in conflict with our background of religious training and beliefs—and with these there is certainly no quarrel. Medicine has no place without conscience, and the doctor who does not practice within the confines of his conscience has no place in the profession. But for others of us the problem remains trying and difficult.

One solution lies in the giving of advice on contraception, but for the patient for whom this is impractical or ineffectual we have only the alternative of operative sterilization. This procedure should not be undertaken lightly. Its very permanence, along with the occasional complication such as later psychosis, makes it one to be considered most carefully, even after a full and detailed explanation of all possible facets has been given the family. And yet toward the family of excessive multiparity, already overburdened with economic, medical, and social problems, an attitude of something more than apathy should be expected of the physician. It is not easy. His lack of legal protection in the light of his natural conservatism usually makes him a reticent participant even though the instigation comes, as it should, from the family.

Since soul-searching, like charity, should begin at home, a critical survey of our own activities in a portion of the city of Greensboro was undertaken. Thanks to the generous cooperation of all doctors concerned, full facts and figures for one hospital are available. One hundred and thirty female sterilizing operations were done at the Moses H. Cone Memorial Hospital during the 40 month period from April, 1953, through July, 1956, as shown in Table V. The total number of pregnancies which preceded these 130 operations was 673, an average of 5.1 per individual. The highest number was 18 and the lowest 1, this latter patient being sterilized for imbecility by order of the Eugenics Board. Four thousand seven hundred and seventy-five (4,775) deliveries were recorded during the period of this study.

TABLE V. INDICATIONS FOR TUBAL LIGATION

Multiparity	54
Some form of toxemia	16
Severe varicosities	15
Previous section with thin scar	11
Hernia or prolapse	10
Rh sensitization	5
Cardiac disease	5
Tumors	3
Epilepsy	2
Other	9
Total	130

This discussion is not intended as a plea for either a greater or a lesser number of tubal ligations. It is rather a plea for a more careful consideration of our responsibilities to the patient in the light of present-day legal, ethical, and moral standards.

It is my strong belief that the rights of individuals who desire family limitation are frequently ignored or neglected. This is not the fault of the physician, but can be attributed rather to the conflicting maze of legal ambiguities which confuse hospital, doctor, and patient alike. When we consider that only a very few of these operations had any legal standing whatever, the situation appears truly distressing. North Carolina, like a great many other states, takes no positive legal stand but continues to operate negatively under the

Old English law concerning mayhem. In effect, the destruction of any normal tissue becomes a felony and the patient herself has no right to give consent to any mutilating procedure.

As a curious incongruity, the state has wisely set up a Eugenics Board which may authorize sterilization for the mentally defective. This Board functions well, and no criticism of its activities is intended. But while the state is undoubtedly correct in denying to the feeble-minded and mentally retarded the privileges of procreation, by what authority does it deny the person of a sane mind the prerogative of family limitation?

Conclusion

In conclusion, I believe that all of us should come to a fuller realization of the importance of family expansion and family limitation which may frequently be of such vital concern to our patients. Though time consuming and as a rule financially unrewarding, the responsibility is one which we should not care to lose. It is our peculiar privilege to have been entrusted with the abilities and skills which enable us to correct a portion of these difficulties. It we are willing to add to these a measure of patience and understanding, the results in achievement and in personal satisfaction may well exceed our expectations.

THE SPATULES OF THIERRY*

JULIO ORTIZ PÉREZ, M.D., HAVANA, CUBA

(From the Lying-In Department of the Calixto García Hospital, University of Havana)

IT IS perhaps a presumption to endeavor to replace the obstetrical forceps. Nevertheless, Dr. E. Thierry, of Rouen, France, has designed and used for the last ten years an instrument, the spatules, which does precisely that.

First made known to the medical world in 1950, they have been used by me since 1953. At present I resort to the forceps only for the directly posterior (O.P.) heads, not spontaneously resolved. In all other cases I employ the spatules exclusively. More especially as a substitute for prophylactic forceps, the spatules have been of great service.

The spatules themselves are two independent levers (Figs. 1 and 2). Each one consists of a blade, a shank, and a handle. The blade is unfenestrated and of ample size, being a little more than 4 cm. at its widest part. It shows a not very marked cephalic curve and a slight pelvic curve, designed apparently to facilitate its manipulation. The total length of each lever is 40 cm.

The spatules are based on a principle entirely different from that of the forceps. They do not have a lock and are always completely independent. With them there is a certain amount of slipping but, if they are properly applied, scraping is impossible. This slight slipperiness separates them from the cranium which they are unable to compress but for which they serve as a means of protection. Instead of pulling the head, they rather push or propel it.

The spatules are two primary levers and, in order to function, the outer faces of the blades rest on the inner surfaces of the pelvic bones. In no way may they constitute a pair of pincers as do the obstetrical forceps. The spatules act on the sides of the fetal face to press the presenting part forward and to further its flexion and rotation. In using the spatules one has the impression of the head being free.

In transverse presentations the posterior blade functions as a sliding plane while we rotate the head with the anterior blade.

The spatules are applied in the same manner as the forceps. A blade is placed on each side of the face of the fetus. The handles must be kept parallel or with a very slight divergence. Traction is made by the handles and should try to follow the mentosupraoccipital diameter.

In order to rotate the head, the posterior spatula is held firmly or with very slight traction, while the handle of the anterior spatula is raised and moved toward the center; thus the distal end of the blade acting on the fetal face

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makes the rotation of the head. On occasions this maneuver has to be repeated two or three times in order to bring the head to a complete anterior rotation.

In my opinion the spatules can never inflict any injury on the head of the fetus, such as may occur on some occasions with the forceps. I have employed the spatules more than 300 times and up to now I have been entirely satisfied with them though naturally I have not yet put away my forceps for good.

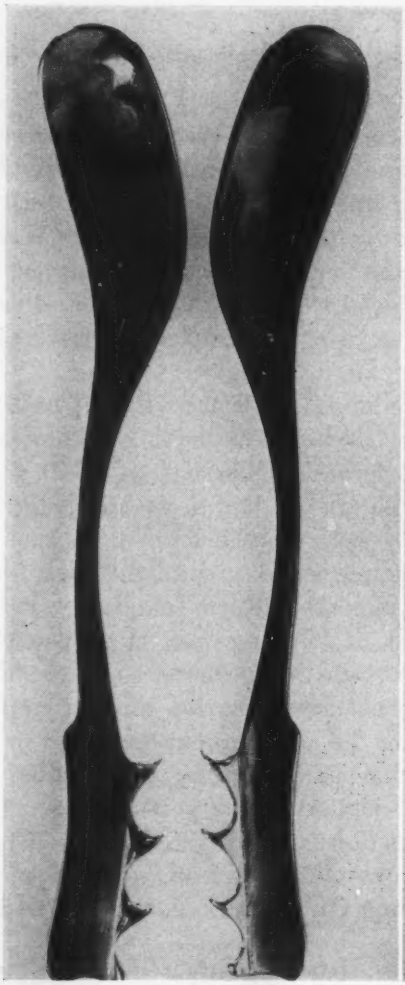

Fig. 1.

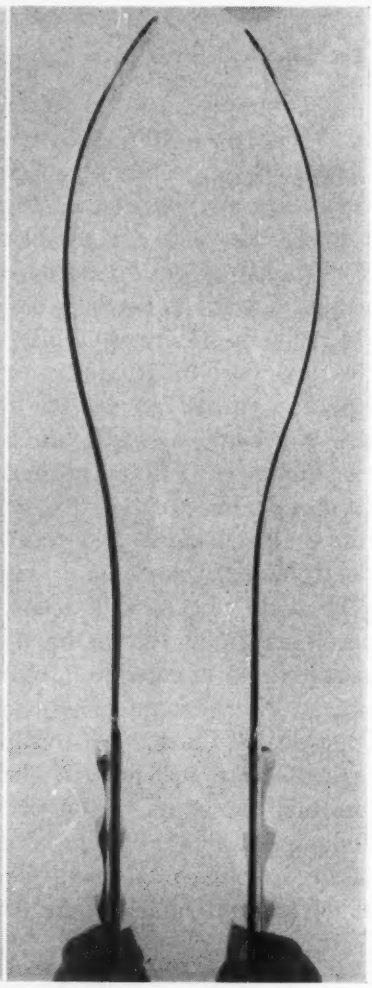

Fig. 2.

Fig. 1.—Photograph of the spatules of Thierry seen from the side.
Fig. 2.—Photograph of the spatules on edge to show cephalic curve.

Discussion

DR. JULE C. NEAL, JR., Macon, Ga.—We have had no experience with Dr. Thierry's spatules in our hospital, a city-owned, private and charity institution. We had 20,699 deliveries in the past 5 years, of which 2,840 were forceps deliveries—approximately 1,250 done by one physician. Of the 1,590 remaining forceps deliveries, 1,284, or 6.2 per cent, were so-called low forceps including prophylactic forceps, so that our forceps problem is not that of some similar institutions.

Dr. Thierry's spatules and the description of their use bring several thoughts to mind: First, it must take much practice to become adept in propulsion of the head. Second, since they are levers, and the fulcrum is the pelvic bones, is there not a great deal of damage to the soft tissue of the vault? Third, since the spatules work independently and separately, it must be difficult to accomplish the episiotomy where no help is "scrubbed" in the usual delivery.

DR. JOHN R. SAUNDERS, Lynchburg, Va.—It seems to me that this instrument has several desirable features: (1) Compression of the baby's head is practically eliminated. This should prevent many of the hematomas under the scalp, which we encounter too often in routine outlet forceps deliveries done with the conventional instruments. (2) Rotation done with the anterior blade is of a distinct advantage, as it should do away with the damage to the maternal soft parts, often experienced when the Scanzoni maneuver or the Kielland forceps are used for this purpose. (At this point I would like to emphasize that a manual rotation has proved for me to be the safest and most effective method of dealing with a transverse arrest or a persistent posterior. It is almost impossible to injure the cervix or vaginal tissues when this method is used.) (3) The lack of a locking device on these blades should make it possible to propel the baby's head along the birth canal even when a perfect application has not been obtained. With conventional types of forceps the exertion of traction when the blades are not well locked usually ends in failure and also if pursued can do considerable damage.

I would like to see this instrument demonstrated on a manikin in order better to understand its use.

DR. BAYARD CARTER, Durham, N. C.—Dr. Perez stresses that the spatules are primary levers and that in no way do they constitute a pair of pincers as do obstetrical forceps. His opinion that the spatules can never inflict injury to the head of the fetus is held in high respect since he has used the spatules in more than 300 cases.

Certainly we must regard his presentation today as a stimulus to us to try the spatules and to determine for ourselves how best to manage the obstetric problems which in his hands the spatules have helped to solve.

THE MANAGEMENT OF ABRUPTIO PLACENTAE*

LAWRENCE L. HESTER, JR., M.D., AND JULIAN SALLEY, M.D.,
CHARLESTON, S. C.

(From the Department of Obstetrics and Gynecology, Medical College of South Carolina and Roper Hospital)

PREMATURE separation of the normally implanted placenta, accidental hemorrhage, ablatio placentae, or, as here designated, abruptio placentae has long been recognized as one of the most serious complications of pregnancy. This study is directed toward an evaluation of the conservative management of this obstetrical catastrophe and some of its common complications.

There is disagreement among obstetricians regarding the clinical management of the moderate and severe cases of abruptio placentae. Most agree that the majority of these patients can be delivered successfully by the vaginal route; however, some advocate liberal use of abdominal delivery, while others subscribe to more conservative management, restricting the use of cesarean section to the occasional case. Thus Page,[1] reviewing cases of abruptio placentae on three separate services found a cesarean section rate of 10.4 per cent and 14.8 per cent in two hospitals while the section rate was 51.6 per cent in a third. Eastman[2] reported a cesarean section rate of 37.7 per cent while Daro,[3] Studdiford,[4] and Tatum[5] each reported a cesarean section rate of approximately 12 per cent. We have been consistently conservative at the Medical College of South Carolina, using cesarean section only in an occasional case. Recently, it was decided to review the last 100 cases of abruptio placentae to evaluate the results with this therapy. These cases represent only service patients, and they were treated by a consistent regime. These 100 cases of abruptio placentae occurred in 7,434 deliveries, an incidence of 1.3 per cent or 1 case to every 74 deliveries.

Since the maternal and fetal prognosis, as well as the method of treatment, varies markedly with the severity of the disease, the 100 cases have been divided into groups of severity according to the classification of Page.[1] We agree with him that a clinical classification according to recognizable maternal symptoms has much to be desired over other methods of classification. Page's system of grading severity is as follows:

Grade 0.—These are clinically unrecognized before delivery. (Diagnosis is based upon examination of placenta).

Grade 1.—These show external bleeding only, or mild uterine tetany, but no evidence of maternal shock.

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*Presented at the Nineteenth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Charleston, S. C., Feb. 6 to 9, 1957.

Grade 2.—In this group there is uterine tetany, ordinarily with uterine tenderness, possibly external bleeding, fetal distress (or death), but no evidence of maternal shock.

Grade 3.—Here there is evidence of maternal shock or coagulation defect, uterine tetany, and intrauterine death of fetus.

In our series of cases Grade 0 were not considered. The 100 cases were classified according to severity as follows: Grade 1, 37; Grade 2, 38; Grade 3, 25.

Toxemia

Toxemia was present in a high percentage of cases, namely, 45 per cent. In cases of Grade 1 severity, pre-eclampsia was most common, whereas in Grade 3, hypertensive vascular disease with superimposed pre-eclampsia was most frequent (Table I). The classification of toxemia as recently revised by the American Committee on Maternal Welfare and the criteria for the diagnosis of each class were used in determining the incidence. Thus, patients with a blood pressure of more than 140 mm. of mercury systolic and 90 mm. of mercury diastolic at some point during labor were not included. Also proteinuria of 3 and 4 plus was present on admission or soon after the separation occurred in many cases of abruptio placentae of Grade 3 severity, but again these were not classified as toxemia of pregnancy if no evidence other than this transient proteinuria was present. Bartholomew[6] feels that toxemia is often initiated during labor with proteinuria as a result of degeneration of the chorionic epithelium. Others feel that proteinuria associated with abruptio placentae is not evidence of pre-existing toxemia, but suggests that some hours have elapsed since the separation occurred. The mechanism of this renal effect in abruptio placentae is not established clearly; but it was seen in many of the severe cases in this series, and disappeared shortly after delivery. It is interesting to note that there was a higher percentage of toxemia in abruptio placentae of Grade 2 severity than of Grade 3, and for this we have no explanation.

TABLE I. INCIDENCE OF TOXEMIA BY DEGREE OF SEVERITY

	PRE-ECLAMPSIA	HYPERTENSIVE VASCULAR DISEASE	HYPERTENSIVE VASCULAR DISEASE WITH PRE-ECLAMPSIA	TOTAL
Grade 1	9	1	0	10 (27%)
Grade 2	15	8	1	24 (63%)
Grade 3	4	1	6	11 (44%)

Treatment

Treatment of the 100 cases of abruptio placentae was directed by a uniformly conservative group of obstetricians and gynecologists. The basic regime consisted of replacement and supportive therapy, amniotomy in the moderate and severe grade of abruptio placentae irrespective of the favorable condition of the cervix, and in an occasional case, Pitocin stimulation. In the entire group of 100 cases of abruptio placentae, only 3 cesarean sections were performed. Two of these were performed on patients who had had previous cesarean sections and only one operative delivery was performed for the single indication of abruptio placentae. This patient had massive uncontrolled antepartum hemorrhage associated with the severe abruptio and a Couvelaire uterus. Table II summarizes therapy according to the grade of severity. Amniotomy was performed consistently in moderate and severe grades unless there had been a

previous spontaneous rupture of the membranes confirmed on sterile pelvic examination, or a delay in diagnosis. The few cases in which Pitocin stimulation was used are statistically insignificant. There were no complications associated with its use, and delivery appeared to be hastened in each of the 8 cases.

TABLE II. TREATMENT OF ABRUPTIO PLACENTAE

	AMNIOTOMY	PITOCIN	CESAREAN SECTION
Grade 1	12	0	0
Grade 2	28	4	2
Grade 3	21	4	1

Fetal Mortality

There were 102 infants delivered in our series of 100 cases since there were 2 sets of twins. The perinatal mortality was 68 per cent, which is higher than that usually reported. This high perinatal mortality can be accounted for by the fact that fetal heart tones were absent in 50 per cent of the patients on admission and that there was such a high percentage of cases that were Grade 3 in severity. Most of the neonatal deaths were associated with prematurity, the incidence of which was 58 per cent.

In the Cases of Grade 1 severity there were 10 perinatal deaths, although fetal heart tones were present in all cases on admission (Table III). Six of these deaths were neonatal and 4 were stillbirths. All but 2 of the perinatal deaths occurred in premature infants; 7 of 8 weighed less than 2,000 grams. Of the 2 term infants lost, one was anencephalic, and the other one died of unknown causes. No autopsy was performed.

TABLE III. FETAL MORTALITY—100 CASES, 102 INFANTS

	PERINATAL MORTALITY	PREMATURITY
Grade 1	10 (27%)	51%
Grade 2	34 (87%)	72%
Grade 3	25 (96%)	46%

In cases of Grade 2 severity there were 34 perinatal deaths and 5 infants surviving. These moderately severe cases of abruptio placentae appear to be the most favorable for improvement in fetal salvage since the clinical diagnosis is usually made with a high percentage of accuracy and the fetus may be alive when the diagnosis is made. With this fact in mind, we reviewed these cases in some detail in the hope of finding a means of increasing fetal salvage. The findings were not particularly enlightening in this respect, in that fetal heart tones were absent on admission in 28 of the 38 cases. That left only 10 babies in this group that were theoretically salvageable. Five of these survived, 4 were delivered by amniotomy and conservative therapy and one by a repeat cesarean section. Of the 5 infants that were lost, in 4 cases the fetal heart tones disappeared within minutes after the patients were admitted to the ward and before any definitive therapy could be carried out. The fifth case was associated with delay in accurate diagnosis and an early delivery by amniotomy or cesarean section would undoubtedly have prevented this fetal death.

There were 3 cases which progressed from Grade 2 to Grade 3 after admission and were classified as Grade 3 in severity. In all of these, fetal heart tones were present on admission, and in 2 of the cases they were present for a sufficient time for a cesarean section to be contemplated and performed. Theoretically early operative interference may have saved these 2 babies; however, in both cases the diagnosis was in question until fetal death in utero occurred.

There seems, therefore, to be little to offer in respect to increasing fetal salvage except earlier, accurate diagnosis and the institution of earlier therapy, be it amniotomy or cesarean section. In private practice there should be a higher incidence of cesarean section for fetal salvage in the moderately severe cases of abruptio placentae since there will be a decreased patient delay in securing medical care.

Maternal Complications

In this series of 100 cases there were 12 cases of postpartum hemorrhage and 9 cases of puerperal morbidity due to endometritis (Table IV). The 12 per cent incidence of postpartum hemorrhage is not unusually high and it is to be noted that none of the maternal deaths were caused by postpartum hemorrhage.

TABLE IV. MATERNAL COMPLICATIONS

	POSTPARTUM HEMORRHAGE*	PELVIC INFECTION	HYPOFIBRINOGENEMIA	ACUTE RENAL FAILURE	DEATH
Grade 1	2	2	0	0	0
Grade 2	4	5	0	1	2
Grade 3	6	2	3	2	2

*Not associated with clotting defect.

The complications of hypofibrinogenemia and acute renal failure were not related to the factor of delay in delivery except in Case 3 to be described below (Table V). Early vaginal delivery is, however, desirable and preferable. Severe hypofibrinogenemia was diagnosed and combated effectively with fibrinogen in 3 patients. Acute renal failure was present in 3 cases.

TABLE V. RELATION OF DURATION OF ABRUPTIO PLACENTAE TO COMPLICATIONS

	HYPOFIBRINOGENEMIA			ACUTE RENAL FAILURE		
	CASE 1	CASE 2	CASE 3	CASE 4	CASE 5	CASE 6
Onset and delivery (hours)	4½	3	10	5	6	4
Amniotomy and delivery (hours)	1	3	3	1	2	2

Two deaths were associated with abruptio placentae of Grade 2 severity and 2 with Grade 3 severity. The 4 per cent maternal mortality rate compares favorably with that in other reports[1, 6, 7] when corrected according to the severity of the disease in the cases reviewed. Two of the 4 maternal deaths occurred in cases of abruptio placentae of grade 2 severity and were not directly related to the abruptio, but rather to other serious obstetrical complications, since both patients died of cerebral-vascular accidents complicating severe toxemia of pregnancy in which the small separation seemed of secondary importance. The 2 deaths in abruptio placentae of Grade 3 severity were directly attributed to the separation of the placentas. Both deaths were due to renal failure with uremia. Since both of these patients were delivered within 4 hours of the onset of abruptio placentae and within 2 hours after admission to the hospital and amniotomy, it seems unlikely that cesarean section would have prevented these deaths.

Maternal Deaths

The maternal deaths are briefly summarized as follows:

CASE 1.—A 33-year-old gravida xi, para ix, abortion i, 36 weeks pregnant, was admitted with the signs and symptoms of severe abruptio placentae. Her previous pregnancy was complicated by hypertensive vascular disease and chronic pyelonephritis and terminated in abruptio placentae and a stillbirth. On this admission pre-eclampsia was superimposed on

hypertensive vascular disease. She was delivered 2 hours after admission, and 1 hour after amniotomy. She received 1,000 c.c. of whole blood after delivery, anuria developed immediately, and the patient died of uremia secondary to acute renal failure on the tenth postpartum day. Pathological examination of the kidneys revealed bilateral renal cortical necrosis.

Comment.—This patient was never in shock and received vigorous and adequate treatment.

CASE 2.—A 34-year-old gravida viii, para vii, was admitted at 32 weeks' gestation, having had no prenatal care. She gave a history of sudden severe abdominal pain one hour before admission and physical examination disclosed the findings of severe abruptio placentae. Amniotomy was performed, and delivery occurred 4 hours after the separation occurred. This patient received only 500 c.c. of blood prior to delivery; however, she was in and out of shock several times. Death occurred on the eleventh postpartum day of uremia, although diuresis was present for 24 hours. Autopsy was denied.

Comment.—This patient was delivered 4 hours after the onset of abruptio placentae and 2 hours after amniotomy. The acute renal failure and death might have been prevented by adequate blood replacement which the patient did not receive.

CASE 3.—A 22-year-old gravida i, para 0, abortion 0, unregistered Negro woman, was admitted at 34 weeks, gestation because of intermittent abdominal pain. The patient was delivered of a premature stillborn infant weighing 2 pounds, 6 ounces, 2 hours after amniotomy. Just prior to delivery her blood pressure increased to 240/125 with progression into a comatose state. Death occurred 27 hours post partum and the pathological report was "eclampsia with pituitary, adrenal, and hepatic necrosis. Glomerular and tubular degeneration of the kidneys and cerebral hemorrhage."

Comment.—Death resulted from a cerebral-vascular accident and the abruptio placentae seems of secondary importance. Perhaps vigorous antihypertension therapy was indicated and might have prevented this death.

CASE 4.—A 23-year-old gravida i, para 0, was admitted to the ward at 20 weeks' gestation because of severe hypertension. Her condition was evaluated and it was the impression of the Medical Department that the patient had a congenital auricular septal defect with superimposed bacterial endocarditis and focal glomerulonephritis. Also, the possibility of a pheochromocytoma was entertained. The patient died 70 days after admission of acute pulmonary edema immediately following delivery of a premature stillborn infant. It was suspected that the intrauterine death may have been associated with a small separation of the placenta although there was no uterine tenseness and only slight external bleeding. A small area of placental separation was noted at delivery. The final pathological diagnosis was myocardial hypertrophy and generalized arteriosclerosis, with arteriosclerosis of the kidneys and early necrosis, and questionable pheochromocytoma.

Comment.—Again abruptio placentae seems of secondary importance and contributed little if any to the maternal death.

Comment

Diagnosis of abruptio placentae is usually obvious except in Grade 0 and Grade 1 severity; however, plans for diagnosis and treatment of third-trimester bleeding must be initiated as soon as the patient is admitted to the ward. Grade 2 often progresses to Grade 3. General physical examination on admission should include a measurement of the height of the fundus from the symphysis pubis and the girth of the abdomen so that any increase in the size of the uterus from concealed hemorrhage may be detected. Venous blood should be obtained through a large-caliber needle for immediate complete blood count and volume of packed cells, and the patient's blood should be typed and crossmatched for at least 1,500 c.c. of whole blood. Clotting time and "clot observation tests" should be done immediately and hourly until the patient is delivered

or as long as indicated. Blood fibrinogen determination is preferred if available. With the same needle, glucose in water should be started so that a large vein is readily available if transfusion becomes indicated. Oxygen is started per nasal catheter, a physician is in constant attendance, and the blood pressure is checked and recorded every 5 to 15 minutes.

If clinically and on sterile pelvic examination abruptio placentae is diagnosed, the treatment for each grade of severity is briefly as follows:

Grade 1.—Bedrest and observation except in a patient with a near- or at-term fetus and a ripe cervix; then amniotomy is indicated. Blood replacement only if bleeding is excessive.

Grades 2 and 3.—Oxygen, blood replacement, amniotomy, and in certain selected cases a Pitocin infusion. Fibrinogen is made available. Cesarean section for fetal salvage in Grade 2.

The cesarean section rate for abruptio placentae was 3 per cent in our series, which is less than the ward rate of 3.5 per cent. One section was for uncontrolled hemorrhage, another for fetal distress in a patient with a previous section, and the third for questionable uterine rupture associated with a uterine scar from a previous abdominal delivery. Cesarean section is indicated for fetal distress and uncontrolled hemorrhage in addition to the usual obstetrical reasons. From this study, cesarean section did not appear indicated merely to reduce the interval between the time of onset of abruptio placentae and delivery, although ideally delivery should be accomplished in 4 to 6 hours after the separation. In this series, of the 50 patients with abruptio placentae of Grade 2 or 3 severity who did not exhibit the previously mentioned maternal complications (Table IV), only 19 were delivered in less than 6 hours, and 31 were delivered in more than 6 hours after the occurrence of the abruptio placentae, while the patients with the complications were delivered rather promptly (Table V). Cesarean section did not appear justified to secure delivery after maternal shock had been successfully combated, except for the indications previously mentioned. The policy of some clinics that abdominal delivery is necessary to empty the uterus if delivery does not occur in a stated number of hours appears unjustified. This policy has been further modified in smaller hospitals, especially those without obstetricians and gynecologists on their staffs, to the effect that vaginal bleeding in the third trimester of pregnancy is an indication for cesarean section.

Amniotomy is essential to hasten delivery and to decrease the intrauterine pressure and thus the danger of hypofibrinogenemia from an infusion of thromboplastin. Even in the presence of an unfavorable cervix, amniotomy is usually followed by a rapid labor and delivery. In 5 cases in this series in which the cervix was relatively unfavorable (thick and 1 to 2 cm. dilated) the average time from amniotomy to delivery was 6 hours and 48 minutes. In 11 cases in which the cervix was favorable (50 per cent effaced and 3 to 5 cm. dilated), the average time from amniotomy to delivery was 3 hours and 30 minutes. If labor is poor following amniotomy, however, and there is no contraindication, Pitocin (1 minim to 100 c.c. of 5 per cent glucose in water) intravenously was helpful in hastening delivery. Abruptio placentae did not appear to be a contraindication to Pitocin therapy as has been suggested by others.[1]

Blood loss should be combated with whole blood transfusions until the replacement is considered adequate. Retroplacental bleeding is difficult to estimate, thus the maternal blood loss may be underestimated and adequate replacement not given. It must be remembered that rapid labor cannot be expected to occur if the patient is left in shock and is hypovolemic. If these deficiencies are corrected, the uterine contractions will usually be strong and effective, resulting in an unusually short labor.

Conclusions

1. One hundred consecutive ward cases of abruptio placentae treated conservatively are presented.

2. The cesarean section rate was 3 per cent, the indications being fetal distress, uncontrolled hemorrhage, and a previous cesarean section.

3. An increased incidence of cesarean section to reduce the elapsed time from placental separation to delivery does not appear to have reduced maternal complications in this series.

4. Fetal salvage in this series would have been increased only slightly, if at all, by a more liberal use of cesarean section.

References

1. Page, E. W., King, E. B., and Merrill, J. A.: Obst. & Gynec. 3: 385, 1954.
2. Eastman, Nicholson J.: Williams Obstetrics, ed. 10, New York, 1950, Appleton-Century-Crofts, Inc., p. 586.
3. Daro, A. F., Gollin, H. A., Nora, E. G., Jr., and Primiano, N.: Am. J. Obst. & Gynec. 72: 599, 1956.
4. Studdiford, W. E., and Decker, Wayne H.: Obst. & Gynec. 1: 418, 1953.
5. Tatum, T. J.: Obst. & Gynec. 2: 447, 1953.
6. Bartholomew, R. A., Calvin, E. D., Grimes, W. H., Fish, J. S., and Lester, W. M.: Am. J. Obst. & Gynec. 62: 246, 1951.
7. Sexton, L. I., Hertig, A. T., Reid, D. E., Kellogg, F. S., and Patterson W. S.: Am. J. Obst. & Gynec. 59: 13, 1950.

Discussion

DR. JULIAN C. BRANTLEY, JR., Rocky Mount, N. C.—Dr. Hester's analysis of the material presented leaves no doubt that the outcome of conservative management of premature separation of the placenta, as outlined, could have been improved upon little, if any, by resorting to the more frequent use of cesarean section. I agree that only in rare exceptions will abruptio placentae of Grade 1 or Grade 3 severity be more profitably managed by cesarean section. It is in the intermediate group that conjecture arises regarding the method of management, with especial regard to fetal salvage.

In the material presented, in 32 of 38 cases in the intermediate group, fetal heart tones were either absent on admission or were lost "within minutes." Five infants survived, the fetal loss being 87 per cent. This left only one that might have been saved. In the work by Page referred to in Dr. Hester's presentation, fetal loss in the intermediate group was 67 per cent for vaginal delivery and 21 per cent for section. It immediately becomes apparent that these authors are dealing with different classes of patients or there is a discrepancy in the grading of them.

The problem of grading patients with abruptio placentae, according to degree of severity, is not always simple. There is frequently room for individual differences in interpretation of the findings in a given case. Though only a small percentage of Grade 1 cases progress to the more severe variety, all of the severe cases must begin in a milder form. It is in this stage of transition from the mild to the more severe form that action must be taken

if the infant is to be saved. Here cesarean section has its place. Unfortunately, even with the patient under observation, the transition is often so rapid and explosive that salvage of the infant is impossible.

It would be interesting to know the actual duration of delay in Dr. Hester's series of cases of the intermediate group, in view of the high percentage of intrauterine fetal deaths on admission. It would also be of interest to know the number considered to have had adequate prenatal care. In the indigent class patient here presented, it appears there is little hope for improvement in the outcome for either mother or child except through education and its corollary, adequate prenatal care.

DR. GEORGE R. JONES, Richmond, Va.—The incidence reported by Dr. Hester of only one cesarean section performed primarily for abruptio placentae is certainly surprising. The authors do recognize, however, that in private practice there should be a higher incidence of cesarean section for fetal salvage in the moderately severe cases of abruptio placentae, since there will be a decreased patient delay.

In reviewing their results on fetal mortality, I cannot offer any suggestion on how these babies could have been saved. The only child that possibly could have been saved by cesarean section in Grade 1 was the infant that died of unknown causes with no autopsy being performed.

In my opinion, the maternal deaths in this series could not be prevented. The 2 patients who died of renal failure with uremia were delivered rapidly and I believe properly.

In the classification of abruptio placentae we should think constantly of abnormalities in blood clotting. While undelivered, the patient is in constant danger from incoagulable blood, but once she is delivered, the coagulation factors do not decline further.

Most patients can and should be delivered vaginally. Artificial rupture of the membranes reduces intrauterine pressure and prevents further defibrination of the blood. If delivery is unduly delayed I believe cesarean section is indicated.

In managing abruptio placentae, I believe one should definitely consider cesarean section in the following cases:

1. Labor of longer than 10 to 12 hours.
2. Excessive antepartum hemorrhage which cannot be readily combated by transfusions provided the fibrinolytic syndrome is not present.
3. In Grade 2 if fetal heart tones are present.
4. In milder separation if labor fails to transpire within 6 to 12 hours after rupture of the membranes, or if bleeding is not controlled by amniotomy or if further separation threatens fetal life.
5. In severe separation after the initial shock has been alleviated and the clotting mechanism restored to normal, cesarean section seems preferable to an unpredictable and possibly exhausting labor in a patient recently recovered from shock.
6. At the first sign of fetal distress in an infant estimated at more than 2,000 grams delivery should be immediate.

DR. C. PAUL HODGKINSON, Detroit, Mich.—We also have found it difficult to gain as much information as we would like from reviewing cases in retrospect. Fibrinogen seems to be the key to the situation. In observation of cases in the last few years, we have done extensive fibrinogen studies and have been amazed to find that any patient who had any proved degree of abruptio placentae showed some evidence of fibrinogen depression. I think it presents a very real and potentially serious problem. I commend to you wholeheartedly the use of the "clot observation test" which is a practical test anyone can do in the delivery room.

The question as to whether or not one should perform a cesarean section is an individual problem. Mostly, the decision is based upon the firmness of the cervix. If the cervix is soft, and one gets the idea that the patient will be delivered quickly, I believe vaginal delivery is to be preferred. Of course, a long, difficult labor is to be avoided, even in the presence of a fetus known to be dead. Cesarean section, therefore, I believe, can be done for both fetal and maternal reasons. As one of the discussants mentioned, the fibrinogen depression is reversed once the baby is delivered.

Very recently a patient was admitted to our hospital about 2 o'clock in the morning with frank symptoms of abruptio placentae. Fibrinogen studies were initiated promptly. This patient was not bleeding, she was not in shock, she felt well, she appeared well, the uterus was hard, and the baby was dead. She was multiparous. The membranes were ruptured, and in about 4 hours she was delivered of a recently dead infant. Fibrinogen studies were performed at half-hour intervals. The "clot observation test" was also done. About one hour prior to delivery the patient's blood showed no evidence of clotting. That condition persisted until after she was delivered. Shortly after delivery a small clot formed, soon followed by lysis. As time went on, the clots became increasingly firm and lysis less evident. This patient recovered uneventfully. When we received the reports of the fibrinogen studies the next day, we were shocked to find that this patient's fibrinogen had gone to 40 mg. per 100 c.c. of blood, a level far below the critical level of 90 mg. I call attention to this because it emphasizes a very important fact. Here was a patient whose blood was totally incoagulable, and yet she did not bleed excessively nor did she go into shock. Fibrinogen depression may be subcritical, yet not be apparent clinically.

At the present time, there is a patient who was transferred to Henry Ford Hospital 5 days after cesarean section performed for abruptio placentae, shock, and hemorrhage. She has been anuric since operation. Dialysis has been done twice with artificial kidney and it is remarkable to observe the excellent state in which this patient has continued to exist. Whether or not she will recover, I do not know, but I mention this case because it exemplifies another form of the fibrinogen-fibrin conversion syndrome. Apparently, organs supplied by the arterioles of the end artery type are affected most severely by this form of embolization.

I would like to ask Dr. Hester if any of the patients who developed anuria received fibrinogen. I believe it is possible to overtreat these patients. Administration of fibrinogen in the continued presence of the initiating process may result in precipitation of more fibrin and an aggravation of symptoms.

DR. R. A. BARTHOLOMEW, Atlanta, Ga.—Abruptio placentae and eclampsia apparently stem from the same cause—necrosis of chorionic tissue, but stand in marked contrast as to the possibility of fetal salvage, because of the extreme rapidity with which abruptio develops in the more severe cases. Eclampsia is generally preceded by a gradually increasing toxemia extending over a period of one or two weeks which permits one to induce labor before the symptoms and findings have reached a dangerous level.

Can it be said that there is any possibility of prophylaxis of abruptio placentae since it gives so little warning before it strikes?

Hypertensive vascular disease is outstanding as a factor predisposing to abruptio placentae, whether the disease is latent or already manifest at the beginning of pregnancy. Even early in pregnancy it may be recognized by ophthalmoscopic examination of the retinal arterioles. By practicing on his own patients, the obstetrician may learn to do his own ophthalmoscopy. Normal retinal arterioles are about two thirds the diameter of the accompanying veins and reflect little or no light. If they are found to be noticeably small, expressed as between 1:2 and 2:3 or 1:2, 1:3 or even smaller, and reflect the light more intensely, vascular disease is present. The greater the disturbance in arteriovenous ratio and the intensity of light reflex, the more severe the vascular disease and the earlier in pregnancy hypertension will develop or it will even antedate pregnancy.

Of great significance is the fact that the greater the frequency and degree of vascular disease, the higher the incidence of fulminating abruptio placentae and superimposed preeclampsia. In 1947 (AM. J. OBST. & GYNEC. 57: 69, 1949) over a period of a year, 18 consecutive cases of abruptio placentae were collected from the Negro service of Grady Memorial Hospital, 15 of which showed varying degrees of hypertensive vascular disease—an incidence of 80 per cent. More recently, in 1956, Fish reviewed 10,000 consecutive cases from private practice and found 56 cases of abruptio—1:178. Thirty of these showed hypertensive vascular disease—a frequency of 53.5 per cent, which is five times the normal incidence (AM. J. OBST. & GYNEC. 61: 431, 1951).

Therefore, if one is dealing with a patient who develops a not-too-urgent degree of hypertension and proteinuria in the ninth month of pregnancy but who shows retinal findings

of moderate vascular disease, the feasibility of induction of labor should be assessed from the maternal and fetal standpoints and if the findings are favorable the pregnancy should be terminated, if possible, on account of the increased susceptibility to severe abruptio as well as preeclampsia.

DR. O. HUNTER JONES, Charlotte, N. C.—The accompanying table shows our experience with cesarean section in accidental hemorrhage (including rupture of the marginal sinus) at Charlotte Memorial Hospital since the hospital opened in 1940. During this period of 16 years, almost 18,000 women have been delivered. There has not been a maternal death due to accidental hemorrhage. There has been only one case of known afibrinogenemia. Our staff feels that the liberal and rather early use of cesarean section has helped prevent this complication of afibrinogenemia as well as save babies. Our figures are uncorrected and include all cases of 5 months' gestation and over (since all births at 5 months and over are reportable in North Carolina).

ACCIDENTAL HEMORRHAGE AT CHARLOTTE MEMORIAL HOSPITAL
(5 MONTHS' GESTATION AND OVER)

	1940-1952		1940-1956		1953-1956	
	NO.	%	NO.	%	NO.	%
Cesarean section for accidental hemorrhage	26	20*	47	22*	21	27*
Cesarean section fetal mortality	9	35	11	23	2	9.5

*Per cent of all cases of accidental hemorrhage.

The first part of the table is from the paper on cesarean section I read before this association in 1953. At that time we had performed a cesarean section on 20 per cent of our patients with accidental hemorrhage with a fetal mortality of 35 per cent. When the figures for 1953 through 1956 were added, the cesarean section incidence increased slightly to 22 per cent but the fetal mortality dropped to 23 per cent. Finally if the last 4 years are considered alone, the cesarean section incidence rises to 27 per cent with a fetal loss of only 9.5 per cent (the corrected mortality is zero).

All of you are aware that a number of leading institutions over the country have reviewed their cases of accidental hemorrhage in recent years and many, perhaps most, have come to the conclusion that cesarean section is indicated more often, and certainly earlier, than has been done in the past. Among these institutions are the Sloane Hospital for Women, the New York Hospital, and the Philadelphia Lying-In Hospital. Also, it is the feeling of a great many of us that the use of cesarean section, in properly selected cases and if done early enough, will not only save babies (undamaged babies at that!), but will prevent cases of afibrinogenemia.

As expressed by Bysshe of the Sloane Hospital for Women, New York City, "maternal mortality arises as a consequence of untreated hemorrhage, hypofibrinogenemia, renal failure and anterior pituitary necrosis. . . . All of these secondary complications have been shown to be related to the time lost in emptying the uterus after the original placental separation occurs. . . . In moderate separation, a delay longer than 8 hours enhances the possibility of fetal loss and encourages the development of hypofibrinogenemia."

DR. HESTER (Closing).—What brought this problem to my mind was the high maternal mortality in South Carolina from abruptio placentae. We were amazed at the number of cases that we were studying, through the Maternal Health Committee, of women who either died on the operating table, or died soon thereafter from abruptio placentae treated by cesarean section. Most of these patients did not receive adequate preoperative transfusions, but the deaths were associated with inadvisable cesarean section on poorly prepared patients. I wish to re-emphasize that amniotomy alone is often an effective procedure in accomplishing early delivery.

Dr. Brantley asked about the number of patients who had prenatal care. I think that most of these did not receive prenatal care. They came to the hospital after the abruptio placentae occurred at home.

THE ASSIGNMENT OF SEX TO AN INDIVIDUAL: SOME ENIGMAS AND SOME PRACTICAL CLINICAL CRITERIA*†

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> "Hartford January 1, 1770. We are credibly informed, that about 23 years ago a child was born in the Southern Part of Massachusetts-Bay, who bearing a similarity of both sexes, it was disputed what apparel it should be dressed in, but 'twas at least agreed to dress it in a Women's, and it was baptised by the name of Deborah; this person grew up, and till lately passed for a woman; but having for some time past lodged with one of that Sex, the latter found herself to be with child, and has swore the former to be the Father of it. . . . The consequence has been that they are married together, and the Father instead of his former name, was married by that of Deborah Francis Lewis."
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> From the *Essex Gazette,* Jan. 30, 1770.
> (Quoted in J. Pediat. 47: 790, 1955.)

THE prompt and unequivocal assignment of a sex to a baby at birth is a routine, taken-for-granted, and usually casual formality, based upon a perfunctory inspection of the baby's external genitals. The basic premise is that male-appearing external genitals are matched by Nature with testes and vice versa. When a baby is born with undifferentiated or epicene external genitals (which circumstance has been estimated to occur approximately in 1 out of 1,000 babies[1] or, perhaps, more frequently), assignment of sex no longer is a matter of perfunctoriness and there may rightly be confusion regarding sex certification.

If we accept a correct matching of gonads with the sex assigned upon the basis of external somatic structure as our criterion, then many mistakes have been and are being made, as the subsequent childhood and adolescent course of individuals with morphologically abnormal external genitals amply demonstrates. Putative males and females may not have gonads which are compatible with their assigned sex, because ovarian and testicular tissue may coexist (true hermaphroditism), or because there may occur intrinsic embryological defects of the external genitals (external intersexuality), or because of altered genital morphology resulting from abnormal endocrine activity, as in some individuals with cryptorchidism (male pseudohermaphroditism) and in some with ovaries but with congenital adrenogenitalism (female pseudohermaphroditism).

*Part of the expenses of the studies upon which this report is based was defrayed by grants from the Research Council of Duke University and from Ayerst Laboratories, New York, N. Y.

†Presented at the Nineteenth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Charleston, S. C., Feb. 6 to 9, 1957.

Recent clinical applications of the fundamental observations of Barr and Bertram[2] that there are characteristic differences in the "nucleolar satellites" of the somatic cells of male and female cats, moreover, have indicated that "chromosomal sex" may not conform with the apparent somatic femininity of most individuals with congenital aplasia or hypoplasia of the gonads[3, 4] or with the apparent masculinity of some individuals with congenital degeneration of the seminiferous tubules of scrotal testes[5, 6] or of some with cryptorchidism[7, 8, 9] or with other inherent defects of testicular function.[7, 8] These enigmas have prompted this communication, since data from studies of chromosomal sex otherwise have yielded correlations consistent with gonadal status in male and female pseudohermaphroditism,[10] although 75 per cent of true hermaphrodites have yielded chromatin-positive or gynecoid patterns.[10] It is hoped that some practical clinical criteria for the assignment or reassignment of sex, when morphological incongruities are present, may evolve from the following discussions.

Seven years ago and some years before clinical applications of sex chromatin studies, a group of which I was a member discussed before this society the subject of "Male Pseudohermaphroditism: Some Endocrinological and Psychosexual Aspects."[11] Our discussion dealt primarily with male pseudohermaphrodites, who had been assigned the female sex and who subsequently had been reared as females. This was true of 8 of the 11 patients we reported upon in detail. We observed that those individuals with "gynecoid psychosexual desires and orientation should have these trends furthered by appropriate surgery and by estrogenization" and that "this point of view is in striking contrast to one formerly held: ascertain the nature of the gonads and then fashion the individual as best possible to fit the gonadal sex, regardless of the individual's wishes or possible psychosexual trauma." We noted: "This surgical approach, although it is objective and academic, ignores environmental, social, and psychological components. It results in far more traumatism to the majority of patients than the simple expedient of accepting the sex certified on the birth certificate and requiring that the individual conform to it." The subsequent erudite, comprehensive, and most meticulous studies of a group of psychiatrists at Johns Hopkins Hospital[12-18] have given extended and eloquent confirmation to our views.

What Is Sex?

The antecedent discussion logically poses the question, what is sex? Hampson and associates[18] have discussed "seven variables of sex." These are: (1) chromosomal sex, (2) gonadal sex, (3) hormonal sex, (4) internal accessory genital morphology, (5) external genital morphology, (6) sex of assignment and rearing, and (7) gender and orientation (the psychosexual outlook). The terms "third sex" and "neutral gender," which Masters[19] has applied to aging males and females, obviously do not connote the meanings of sex and gender as employed in this discussion.

Not the chromosomal sex, the gonadal sex, the hormonal sex, the internal accessory genital morphology, or the character of the external genitals is

an accurate point of reference by itself for deciding clinically the sex of assignment and rearing. Furthermore, the sex of assignment and rearing determines to a great degree the gender and orientation of the individual, far more so than the five variables just mentioned. For this reason, if need for reassignment of sex arises, this should be done before gender is well established.

The identification of chromosomal or histological sex is based upon the presence or absence of "nucleolar satellites" in somatic cells. The original clinical technique employed skin biopsy. The presently common method employs oral or buccal smears. Blood or vaginal smears may be used. Indeed, a sex difference in nucleolar structure has been found in cells of many tissues, normal and neoplastic. The simplicity of the method, combined with a false belief that data secured are authentic in recognizing clinical sex, predisposes the test to general use and resulting grave errors of interpretation.

The nucleolar satellite generally is assumed to represent an XX chromosome of female type. The XY male type chromosome is regarded to be too small to provide a characteristic chromatin mass for visual recognition. These assumptions have not been proved with finality. Plunkett and Barr[7] have proposed that the term "chromatin-positive" be used for the "female type" nuclei that contain the sex chromatin and that the term "chromatin-negative" be employed for the "male type" nuclei that lack sex chromatin. They believe that this practice may avoid placing "an unnecessary psychological burden" on the patient. I have objected to reports on chromatin types which have become incorporated into our patient records, reading "studies indicate somatic femininity" or "somatic masculinity." Barr[20] recently has published this significant admonition: "It is premature to equate female-type nuclei with genetic femaleness or male-type nuclei with genetic maleness, as a generalization in errors of sex development, for our present methods give no direct information concerning the genes that are concerned with sex determination and sex differentiation."

Gonadal sex obviously depends upon the presence of testes or ovaries. When both testis and ovary or testis and ovarian tissue coexist, an individual is gonadally bisexual, that is, a true hermaphrodite. Well ingrained in our medical thinking is the concept that the data from surgical exploration and microscopic study of gonads provide the answer of the true sex of an individual with ambiguous or epicene external genitals. This was the basis for Klebs'[21] classification of hermaphrodites in 1876. However, we ask, what is a testis and what is an ovary? Do we decide on structural and histological morphology? Or is the decision based on the fact that the gonad is secreting proper hormones in proper amounts? This cannot be identified by histologic findings: for example, normal-appearing Leydig cells may be estrogenizing an individual. Must a gonad be required to give promise of its characteristic gametic function in order to be identified as a testis or an ovary?

The term "gender" as we shall use it requires explanation. Hampson and associates[18] have stated: "The gender role and orientation of an individual is a term used to indicate all those things that a person says or does

to disclose himself or herself as having the status of a boy or man, girl or woman, respectively. . . . The gender role of an individual is not established at birth as instinctive, nor does it emerge in automatic fashion as though determined by the chromosomes, gonads or other somatic factors. Rather, the gender role is built cumulatively through life experiences encountered and transacted, through casual and unplanned learning, and through explicit instruction and inculcation." Money[12] has observed that "the external genitals are the sign . . . above all others which gives a growing child assuredness of his or her gender. . . . Pubertal changes are signs which either reinforce or lessen a child's assuredness of his or her gender." He also has noted that once gender role is ingrained, "it is never entirely eradicated," and that "not even flagrant contradiction of body functioning and morphology may displace it."

Finally, we face the question, what is an individual's legal sex? Is it the sex assigned on the birth certificate, which is commonly the sex of rearing? Is it the gonadal sex, even though, after gender is well established, pubescent changes or laparotomy findings indicate this to be different from that of certification and rearing? Is the gonadal sex male, when testes are estrogenizing an individual and are not forming spermatozoa? Or is chromosomal sex the legal sex? There will be a further discussion of the medicolegal aspects of ambiguities of sexing when the clinical assignment of sex is considered.

Some Enigmas of Sex

Before discussing in detail the various enigmas of sex, we shall classify some of the ambiguities of sexing and give their characteristics in synoptic form, as follows:

Type 1.—Female pseudohermaphroditism, due to congenital adrenal hyperplasia. Chromatin positive.* Ovaries present; clitoris enlarged and may resemble hypospadic penis; labial fusion may or may not be present; internal genitals gynecoid; precocious android pubescence.

Type 2.—Female pseudohermaphroditism, not due to congenital adrenal hyperplasia.* Due to intrinsically embryological faults or due to maternal virilization during gestation from tumors (as arrhenoblastoma) or androgen therapy. *Chromatin positive.* Ovaries present; clitoris may be penile in size and have penile urethra; labial fusion present; internal genitals gynecoid; gynecoid pubescence. Condition is quite rare, probably approximately 12 reports in the literature, 9 of which are well authenticated.

Type 3.—Male pseudohermaphroditism, with android or ambiguous external genitals and with internal genitals predominantly gynecoid but there may be some android vestiges. Chromatin negative.* Testes abdominal or inguinal; penis large to medium, usually with hypospadias but occasionally with penile urethra; labial fusion present; occasionally may have separate vaginal orifice or urogenital sinus; pubescence usually android.

Type 4.—Male pseudohermaphroditism, with android or ambiguous external genitals and with internal genitals predominantly android but there may*

*Types 1 through 6 may cause confusion as to sex assignment at birth. (Synopsis of these types is amplified and modified from Wilkins and associates.[22])

be some gynecoid vestiges. Chromatin negative. Individuals of this type have otherwise same characteristics as those of type 3, save that pubescence may be android or gynecoid.

Type 5.—Male pseudohermaphroditism, with essentially gynecoid external genitals. Chromatin negative.* Testes abdominal or inguinal; phallus small; no labial fusion; well-formed vulva; usually separate blind vagina; internal genitals predominantly gynecoid but uterus is usually absent or poorly developed; pubescence usually gynecoid.

Type 6.—True hermaphroditism. Approximately 75 per cent chromatin positive.* Gonads may be ovary and testis or contain both ovarian and testicular tissue and usually are (bilaterally or unilaterally) abdominal but may be inguinal or labioscrotal in location; phallus is variable in development; labial fusion variable; internal genitals both android and gynecoid; pubescence may be android or gynecoid.

Type 7.†—Individuals with morphologically gynecoid external and internal genitals who are chromatin negative. This type includes most individuals with Turner's syndrome and those formerly designated as having "ovarian agenesis." Gonads rudimentary or absent; external and internal genitals gynecoid. Sex assignment is unequivocally female. Pubescence does not occur. (This type is regarded by some as the severest form of male pseudohermaphroditism on the basis of the chromatin-negative pattern.)

Type 8.†—Individuals with morphologically android external and internal genitals, save for gynecomastia at pubescence, who are chromatin positive. This type includes the patients with the Klinefelter syndrome who develop gynecomastia at pubescence. Testes are firm and small at pubescence and are characterized by degeneration of the seminiferous epithelium, in the presence of essentially normal-appearing Leydig cells. External and internal genitals are android. Sex assignment is unequivocally male. Pubescence is android save for gynecomastia. (This type is regarded by some as a form of female pseudohermaphroditism on the basis of the chromatin-positive pattern.)

The relative distribution of individuals of types 1 through 6 who confuse sex assignment is interesting and important. We have adapted and combined data reported by Wilkins and associates.[22] These data included those based on records collected from the literature (1895-1950) by Money and upon records from Harriet Lane Home, Baltimore, Md. These composite data are given in Table I.

TABLE I. NUMBER OF INDIVIDUALS OF DIFFERENT TYPES AND DEGREES OF HERMAPHRODITISM (PSEUDO- AND TRUE)*

	SIMULATING FEMALE	SIMULATING MALE	NOT KNOWN	TOTAL
Type 1		168		168
Type 2		9		9
Types 3, 4, 5	49	96	6	151
Type 6	22	11	7	40
Total	71	284	13	368

*Based on records collected from the literature (1895-1950) by Money and upon the records from Harriet Lane Home, Baltimore, Md.[22]

As Grumbach and associates[23] have noted, there is general agreement that "the differentiation of the primordial gonad into a testis or an ovary

*Types 1 through 6 may cause confusion as to sex assignment at birth. (Synopsis of these types is amplified and modified from Wilkins and associates.[22])

†Types 7 and 8 do not cause confusion as to sex assignment at birth. The application of the terms male pseudohermaphroditism and female pseudohermaphroditism to individuals of types 7 and 8, respectively, is regarded by us as unnecessarily cruel and as potentially exposing them to harsh psychosexual traumatism.

is established by the balance of an undetermined number of antagonistic genic determiners carried by both the sex chromosomes and autosomes." Failure of normal differentiation of the gonad may result from fetal disease, maternal disease, or fetal accidents. Failure of local organizers or inductors may contribute to fetal gonadal pathology. The degree of differentiation or suppression of the Müllerian and Wolffian ducts depends upon the presence or absence of functioning fetal testes during the early stages of fetal development. Differentiation of the external genitals may be altered by early function of the fetal testis, congenital adrenal hyperplasia of the fetus, hyperandrogenic conditions in the mother, or by intrinsic embryological defects.

The so-called "monohormonic" theory of morphological differentiation was postulated by Wiesner.[24] Material substantiation of this theory was provided by the experimental studies of Jost.[25-27] This theory is that the presence or absence of the fetal testis is of primary importance in normal sex differentiation, and that, when the fetal testis is absent or does not function during the early stages of fetal life, Müllerian ducts develop and Wolffian ducts are suppressed, the external genitals differentiating in a gynecoid fashion. This theory has supplanted the so-called "dihormonic" theory, based on the classic study of Lillie[28] on the bovine freemartin.

Jost showed that intrauterine castration of female rabbit fetuses had no significant effect upon their sexual differentiation, whereas male rabbit fetuses castrated at an early stage developed female genital ducts, a urogenital sinus, and female external genitals. He found, however, that when male rabbit fetuses were castrated late, essentially normal differentiation of the male genitals was not prevented. Furthermore, he observed that unilateral castration of fetal male rabbits resulted in the development of Müllerian ducts on the castrated side, and of Wolffian ducts on the side of the remaining testis. This indicated that the determinant action of the fetal testis was local and not pervasive, as would be expected if it were hormonal.

Jost's data receive ancillary support from the histological studies on human fetal gonads of Gillman,[29] who found that fetal testes differentiate earlier than fetal ovaries and that their subsequent interstitial-cell hyperplasia indicates possible endocrine activity. Simulant females with gonadal aplasia or hypoplasia and with chromatin-negative patterns apparently provide clinical confirmation of Jost's data. It is assumed that testes fail to differentiate in these individuals and, as a result, there is gynecoid development of the genitals. Grumbach and associates[23] suggest that the preponderance of chromatin-negative individuals in this syndrome indicates that the fetal testis, "particularly its germinal elements, may be more susceptible to damage from some unknown cause in early uterine life than the fetal ovary." Prunty and associates[30] reviewed a group of 9 individuals who had a simulated Turner's syndrome[31] with dwarfing, webbed neck, and other congenital anomalies, but who had normal android morphology. These individuals may be regarded as having a male counterpart of ovarian aplasia or hypoplasia in the female, and it is presumed that their hypoplastic testes were capable of monitoring android differentiation. It has been suggested that these testes did not lack germinal elements.[23]

The finding of anorchia upon careful surgical exploration of morphologically normal males who were presumed to be cryptorchid would seem to negate the clinical application of the data of Jost. However, a logical assumption is that testes were present during the critical period of these individuals' sexual differentiation and that they subsequently degenerated, probably during their descent through the inguinal canals.[23] Gross and Meeker[32] reported upon 5 morphologically normal males with anorchia. Amelar[33] failed to find testes on thorough surgical exploration of a former patient of ours, who we thought had aplastic scrotal testes. This patient did

have islets of Leydig cells along the course of Wolffian duct structures in the inguinal canals. These possibly represent the remnants of degenerated testes.

The finding of Müllerian derivatives in individuals with male pseudohermaphroditism, whose testes show ample Leydig cells, may appear to challenge the sex-differentiating role of the fetal testis. Kozoll[34] reported upon 52 male pseudohermaphrodites, 19 without Müllerian derivatives and 33 with them. Three of our 11 patients[11] had Müllerian derivatives. The explanation of this strange dichotomy is an assumption that there was inhibition of the sex-differentiating function of the testis during the early, critical period of fetal life. There is abundant evidence that these testes do not develop normal gametic function. Their secretory function may be perverse: they may estrogenize individuals, estrogens being secreted in normal gynecoid amounts although daily urinary 17-ketosteroid excretion may be 20 to 30 mg.[23]

True hermaphroditism, despite an apparent nonconformity with the theory that the fetal testis determines sexual differentiation, may provide clinical confirmation of Jost's experiments. When there is an ovary on one side and a testis on the opposite side, differentiation of Wolffian and Müllerian ducts is in conformity with the associated gonad. In those true hermaphrodites with unilateral or bilateral ovotestes, the association or nonassociation of suppression of Müllerian ducts may be assumed to be correlated with noninhibition or inhibition of the sex-differentiating role of the testicular moiety during the early critical period of fetal development. Greene and associates[35, 36] reported the case of a true hermaphrodite of chromatin-positive type (XXY), who was proved to form spermatozoa and to ovulate. They do not regard the experiments of Jost or similar observations of Raynaud and Frilley[37] on mice to establish the causes of human intersexuality.

Another enigma concerns individuals obviously male who have chromatin-positive patterns,[5-9] gynecomastia, well-developed external genitals, and scrotal testes, which, although small, contain Leydig cells and a degenerated seminiferous epithelium. These individuals have been designated as having the Klinefelter[38] syndrome. Bunge and Bradbury[39] have found gametogenesis in a few well-preserved seminiferous tubules of the testes of 3 chromatin-positive individuals with the Klinefelter syndrome. This finding and the one of Greene and associates[35, 36] indicate that spermatogenesis may occur in chromatin-positive individuals. Attention is directed again to the previously quoted admonition of Barr[20] that it is "premature to equate female-type nuclei with genetic femaleness." Despite the original description of the Klinefelter[38] syndrome as typified by characteristic changes in the scrotal testes, azoospermia, hypergonadotropuria, and gynecomastia, subsequent practice has categorized individuals as having the Klinefelter syndrome even when there was no gynecomastia. Findings so far are that the original group with gynecomastia has a chromatin-positive pattern,[5-9] whereas the latter group without gynecomastia is chromatin negative. It is obvious, therefore, that we are dealing with two different syndromes. Nelson[40] has suggested the term "female pseudohermaphrodite with gonadal dysgenesis" for the chromatin-positive individuals with the originally described Klinefelter syndrome and the term "early testicular atrophy due to tubular fibrosis" for the condition found in chromatin-negative individuals (without gynecomastia). We object to the use of the term "female pseudohermaphrodite" to describe these patients who are obviously android and who do not have ovaries. It seems best to continue to use the term "Klinefelter syndrome" to apply to them and to use Nelson's term "early testicular atrophy due to tubular fibrosis" or the

"Nelson syndrome" for the other group. We have also noted our objection to inferring that morphologically gynecoid individuals of type 7, who are chromatin negative, are "male pseudohermaphrodites." We wish that clinical usage were not so well established, but that individuals of types 1 through 6 might be designated by less psychosexually disturbing terms than true and pseudohermaphrodites.

Reconciliation of the morphologically android characteristics and the chromatin-positive status of individuals with the Klinefelter syndrome has been difficult. Nelson[41] has made the following comment: "As I see the situation in the Klinefelter syndrome, the gonads, genetically determined to be ovaries, undergo inhibitory influences at a critical period of development. These influences occur after the medullary component of the gonad has been laid down, but before the cortex has been added. As a consequence, the medullary component proceeds to develop as a testis." This concept, accordingly, does not conflict with Jost's theory of sexual differentiation. Plunkett and Barr[7] have observed: "It seems more likely that the abnormality is the result of a fault in the sex-determining genes in a zygote that bears two X chromosomes . . . the error may lie in the presence of an unusual sex-chromosome complex, such as XXY; but the genetic effect of a chromosome complex of this nature is not known for mammals. Greene et al. (1954) have offered evidence for an XXY complex in a true hermaphrodite with chromatin-positive nuclei." Plunkett and Barr also commented that "the observations on these patients raise, rather than answer, questions." Plunkett[42] has noted: "In some ways the finding of sex chromatin in the above-mentioned males corresponds to the chromatin-negative picture in women with ovarian dysgenesis. Once again this is of diagnostic importance rather than any indication of the most appropriate sex of the individual." Jackson and associates[9] have observed that the chromatin type of these individuals apparently is "at variance with either the validity of the nuclear 'sexing' method" or with Jost's theory of sexual differentiation.

A consideration of female pseudohermaphroditism provides information regarding the mode of action of the fetal testis in sexual differentiation. It has been noted that the action is local and not pervasive, as would be expected if it were hormonal. It is thought that this function is carried out by local organizers or inductors. Certainly it does not simulate the clinically known action of androgens.[23] For instance, in female pseudohermaphroditism due to congenital adrenal hyperplasia, the androgenic effect involves essentially the urogenital sinus and external genitals, the development of the Müllerian ducts being normal. Two female pseudohermaphroditic babies born of mothers[43, 44] with arrhenoblastomas had androgenized external genitals and urogenital sinuses, but no Müllerian alterations. An infant with an enlarged clitoris and scrotumlike swollen labia majora was born of a mother who had received androgen therapy from the fourth month of her pregnancy.[45] Android changes in the external genitals of female babies born of mothers treated with large doses of progesterone to prevent abortion have been observed. These changes may be due to an abnormal conversion of progesterone into androgens, probably due to some quirk in maternal adrenal metabolism. Therefore, adrenal androgens, androgens from arrhenoblastoma, and androgen therapy of the mother appear to alter the urogenital sinus and external genitals of female babies but not their Müllerian ducts.

This discussion has shown that Jost's concept of the role of the fetal testis in sexual differentiation can be applied clinically to the ambiguities of sexing. The mode of this action is apparently through the medium of local organizers or inductors. Overzier[46] has described the following theory: "The

first anlage of the gonads stimulates the first anlage of the *Wolffian* and *Müllerian* ducts, probably even at a time before the anatomical structure can be recognised (Initial Induction). Construction of the male or female duct system follows as a result of Permanent Induction by the further developing gonads. If Permanent Induction is lacking, as after experimental castration in early foetal life or as in *Turner's* syndrome, whether the individual is genetically male or genetically female, the ducts develop in the female direction from the stimulus of the Initial Induction. Yet if Initial Induction is also lacking, as in true agonadism, where there is no gonadal anlage, the *Wolffian* and *Müllerian* ducts persist as co-existing, underdeveloped structures. This theory is supported by experimental and clinical evidence including the author's personal observation of two genetically male siblings with true agonadism—the first cases of this kind in the international literature."

Assignment of Sex

Our discussion concerns those instances when a perfunctory assignment is not permitted by casual inspection of the external genitals at birth.

Sex of Abortuses.—The assignment of sex to an early abortus may not be possible, either because of lack of differentiation of the external genitals or because the abortus frequently may not be available for viewing. Bohle and Heinz[47] have suggested that the chromosomal sex of abortuses might be established from the placenta, portions of which usually are available. Such a study might prove or disprove the thesis that the abortion rate for male fetuses is higher than for female ones. The implantation ratio of male to female pregnancies has been estimated variously to range from 170:100 to 110:100. The birth ratio of boys to girls commonly is said to be approximately 106 to 100.

Determination of Sex Before Birth.—The chromosomal sex of the fetus or baby in utero has been determined by study of the chromatin pattern of cells secured by aspiration of amniotic fluid.[48-50] These findings are of academic interest. The method is not recommended as a diagnostic procedure.

Assignment of Sex at Birth or During the Neonatal Period.—When the appearance of the external genitals is ambiguous, an immediate unequivocal statement as to the sex of the baby may not be possible. The psychological impact on parents of being unable to announce whether they have a boy or a girl may be understandably serious. No statement by the physician should engender any concept that the baby is "half boy and half girl" or is a "morphidite." A kinder explanation is that the baby is "unfinished" or that its genitals are imperfectly formed, and that ultimately some surgical and/or endocrine treatment may be necessary to complete the baby's sexual development. Unfortunately, there is no steadfast or uniformly individual rule for assuaging the anxiety of such parents, for circumventing the intrusion of opinions by nurses or visitors, or for avoiding the gossiping of acquaintances. This fact should stand in bold relief: Individuals with ambiguity of sexing, if they are assigned a practical sex before gender role complicates matters, and if the assigned sex is implemented amply by treatment, should develop into healthy, well-oriented, and sexually adequate, if not fertile, adults.

Bohle and Hienz[47] have reported being able to identify correctly sex at birth by the chromatin pattern of the cell nuclei of the connective tissue and endothelium of the placenta villi. They have suggested that similar studies, when there is confusion about the sex of a baby, might be helpful. Unfortunately, a routine use of the chromosomal test when a baby has ambiguous external genitals does not give necessarily the practical answer, regardless of

whether the test is done on mucosal smears from the baby or upon the placenta. The chromosomal test does not differentiate true from pseudohermaphroditism, although ancillary data may be provided. When a baby with apparently gynecoid genitals is chromatin negative, male pseudohermaphroditism may be expected, if true hermaphroditism and gonadal aplasia or hypoplasia can be eliminated. When a baby with apparently android external genitals is chromatin positive, female pseudohermaphroditism may be assumed, if true hermaphroditism and the Klinefelter syndrome can be eliminated; when such a baby has gonads in the scrotum or in the groins, true hermaphroditism or the Klinefelter syndrome is likely.

When the external genitals appear android and the baby has a chromatin-positive pattern, female pseudohermaphroditism due to congenital adrenal hyperplasia should be the tentative diagnosis, until diagnostic studies eliminate this possibility. Elevated urinary 17-ketosteroid values (2 to 5 mg. per day) establish the diagnosis, since the normal values during the neonatal period are less than 0.5 mg. per day. When the values for urinary 17-ketosteroids are ambiguous, the demonstration of pregnanetriol in the urine confirms the diagnosis of adrenal hyperplasia. When congenital adrenal hyperplasia is diagnosed, sex can be certified definitely as female and effective therapy begun with cortisone. Eventually, and before 2 years of age, clitoridectomy, if necessary, should be done. The result should be a normal and eventually fertile female. Reference to Table I shows that cases of female pseudohermaphroditism due to congenital adrenal hyperplasia outnumber cases of both male pseudohermaphroditism and female pseudohermaphroditism due to other causes.

Having eliminated female pseudohermaphroditism due to congenital adrenal hyperplasia, there would remain for sex assignment babies with male pseudohermaphroditism, true hermaphroditism, or those with female pseudohermaphroditism not due to congenital adrenal hyperplasia. The character of their external genitals would appear to provide a practical, clinical method for sex assignment. Wilkins and associates[22] have expressed an "emphatic opinion that in male pseudohermaphrodites and true hermaphrodites the decision should be made according to the anatomy of the external genitals, without regard to the type of gonad, the chromosomal pattern, or the structure of the internal genital tract." (Reference to their data in Table I indicates that approximately one third of male pseudohermaphrodites and somewhat more than one half of true hermaphrodites would be classified accordingly as females.) Application of this plan, however, would assign all female pseudohermaphrodites whose condition was not due to congenital adrenal hyperplasia to the male sex, despite the fact that these individuals eventually will have a gynecoid pubescence and can be transformed by appropriate surgery into normal-appearing females. The chromatin-positive status of these rare female pseudohermaphrodites might appear helpful in a correct sex assignment; however, approximately 75 per cent of true hermaphrodites are chromatin positive and these latter individuals are more common and almost 50 per cent have android-appearing external genitals. Furthermore, individuals with female pseudohermaphroditism not due to congenital adrenal hyperplasia are often mistaken for cryptorchid males with hypospadias.

Another consideration regarding the external genitals of true and male pseudohermaphroditism is that pubescence may proceed in either a gynecoid or android direction and thereby alter the early prognosis as to the potentialities of the external genitals. It is true that, when the external genitals in male pseudohermaphrodites resemble female ones, the testes of these individuals may subsequently secrete a gynecoid moiety of estrogens, although

their urinary 17-ketosteroid values may be 20 to 30 mg. per day, and eventually a gynecoid pubescence may follow. A similar gynecoid pubescence occasionally may occur in the other types of male pseudohermaphroditism. Furthermore, in patients with male pseudohermaphroditism whose testes do not secrete estrogen, these testes are abnormal and practically never develop spermatogenesis. If ambiguous sexing is associated with the presence of gonads in a normal or bifid scrotum, the male sex usually is assigned, although these gonads ultimately may be proved by biopsy to have mixed elements.

There are those like Lowrie,[51] who recommend that, if the sex is in doubt, the individual should be assigned as male, since when the individual grows up he probably will not marry. On the other hand, there are many who think that, when there is doubt about sex, it is best to assign the individuals as females. The practical idea supporting this plan is that these sexually ambiguous individuals can be transformed into better females than males by appropriate surgery and by endocrine therapy, if necessary. Another consideration is that there is more genital privacy for the female than for the male. It is certainly easier to fashion a cosmetically acceptable and coitally adequate female from a sexually ambiguous individual, than to tailor-make an android-appearing and coitally adequate male, even when the individual has a surgically made scrotum with acrylic gonads or some other type of prosthesis and an improvised urethra that extends almost to the glans of a fairly well-developed phallus or a reasonable facsimile of one. As Wilkins and associates[22] have observed, "to attempt to make a boy of an individual who does not have a fairly well-developed phallus is unwise and condemns the patient to a life of misery."

If the female sex were assigned to all pseudohermaphrodites and true hermaphrodites, including those with female pseudohermaphroditism caused by congenital adrenal hyperplasia (but, of course, not including simple cryptorchidism with or without hypospadias) we would assign correctly all female pseudohermaphrodites and all male pseudohermaphrodites who had gynecoid-appearing external genitals, and thereby we would assign accurately two thirds of all patients with ambiguities of sexing, according to Table I. The remaining one third with android-appearing external genitals (true and male pseudohermaphrodites), with very few exceptions, could not be fashioned into fertile and functionally adequate males; indeed, the ultimate pubescent course of a number of these may have a gynecoid trend.

Despite their previously quoted opinion that the anatomy of the external genitals is the point of reference for sex assignment for individuals with ambiguities of sexing, Wilkins and associates[22] have recommended that, after female pseudohermaphroditism due to congenital adrenal hyperplasia has been eliminated, more extensive studies of the anatomy should be carried out in every patient with ambiguous sexual status. Urethroscopic and vaginoscopic studies are advised, combined with roentgenographic studies following the injection of radiopaque material when additional data are needed. These studies are considered to be indicated when there are deformities of the external genitals, when the external genitals are gynecoid but there are presumed gonads in the inguinal canals or in labial or labioscrotal structures, and in individuals who are apparently cryptorchid with hypospadias.[22] We hesitate to advise these studies on a newborn baby as a prerequisite to sex assignment. These studies will be helpful at a later date in the delineation of the surgical procedures which may be necessary in some individuals.

Wilkins and associates[22] and Gross and Meeker[32] also advise exploratory laparotomy to ascertain the nature of the internal genitals and to define the

gonadal status by gross inspection and by biopsy. Gross and Meeker state that it is their policy, when doubt concerning sex is present, to explore the abdomen within the first few days of life; they emphasize, however, that no corrective surgery should be attempted at this time. Wilkins and associates do not state specifically that exploration should be done so early. We do not advise exploratory laparotomy as a prerequisite to sex assignment. We do regard laparotomy during early pubescence to be essential in the handling of individuals with sexual ambiguities which are not related to congenital adrenal hyperplasia. The purpose of this surgery would be an ample implementation of the assigned sex.

We realize that a highly controversial subject is being discussed We propose, however, an apparent practical plan for the prompt assignment of the sex of rearing for individuals of ambiguous sexing. When an individual has scrotal or labioscrotal gonads and is chromatin negative (the phallus is usually adequate in these individuals), the male sex would be assigned and repair of any hypospadias or urogenital sinus defect would be done as soon as practicable, preferably before school is started. When such an individual is chromatin positive, the male sex also would be assigned and plastic surgery as already mentioned would be done. In addition, the gonads would be subjected to biopsy; if ovarian elements are found, these would be removed. When an individual has cryptorchidism with hypospadias and an adequate phallus, and is chromatin negative, the male sex would be assigned. Before the individual is of school age, the cryptorchid gonads would be subjected to biopsy and, if there were no ovarian elements, an attempt would be made to locate and maintain these gonads in the scrotum. If there were ovarian elements, or if the gonads could not be brought into the scrotum they would be removed.

According to this proposed plan, all the other patients with sexual ambiguities would be certified as females. We would then proceed to make a diagnosis and treat promptly and adequately those with congenital adrenal hyperplasia. The parents of the remaining babies with pseudohermaphroditism and true hermaphroditism would be informed that surgery and perhaps endocrine treatment ultimately would be necessary to complete the sexual development of their babies. The scope of these procedures would be outlined. The parents then would have ample time to discuss the matter with the physician, with a proposed surgeon, and with their spiritual advisers. If, for some reason, they desired to have the assigned sex reversed, this should be done by edict, certainly before the child was 2 years of age. To implement the assigned female sex, an enlarged clitoris or phallus should be removed before 2 years of age. The fashioning of a functional vagina could wait until early pubescence; at this time a laparotomy also should be done and the assigned sex implemented by the removal of testes or ovotestes. It goes without saying that there would be no need of leaving a uterus and cervix in an individual from whom the gonads had been removed or in an individual for whom a connecting vagina cannot be fashioned. Those individuals without gonads would require cyclic estrogen therapy to complete pubescence and for continued genital and metabolic effects.

There may be some medical arguments against removal of abdominal or inguinal testes. It is granted that some of these may secrete estrogen, but this cannot be relied upon or accurately prognosticated. Castration may be postponed until early pubescence but should be done promptly upon the first evidence that the testes are masculinizing an individual. Cryptorchid testes are predisposed to malignant change, however, and should be removed for this reason, whether or not they secrete estrogen. On the other hand, one

should not feel that the removal of cryptorchid testes from an individual assigned female sex is depriving a potential male of fertility, for these testes rarely are capable of spermatogenesis.

There well may be religious objections to the procedures which have been described. There are four applicable Biblical references. Two are in the Old Testament and two are in the New Testament. In Deuteronomy 23:1, we read: "He that is wounded in the stones, or hath his privy member cut off, shall not enter into the congregation of the Lord." If we read no further, the issue would be settled, for this is indeed a very final statement. In Isaiah 56:3-5, it is quite clear that eunuchs are not denied salvation. We doubtlessly are all familiar with this verse from Matthew 19:12: "For there are some eunuchs, which were so born from their mother's womb; and there are some eunuchs, which were made eunuchs of men; and there be eunuchs, which have made themselves eunuchs for the kingdom of heaven's sake." Also, in Acts 8:27-39, Philip's acceptance and baptism of the Ethiopian eunuch is described; accordingly, race, color, previous creed, or castration does not prevent baptism and salvation.

The most perplexing problem is the legal status of these procedures. Armstrong[52] has stated that "the legal determining factor in intersex cases is the anatomic structure of the gonad. . . ." He is uncertain how far a surgeon may go in the implementation of a desired sex. Lowrie[51] has stated that sex *must* be made male if there are testes. Wilkins[53] has observed that "the removal of gonads which are opposed to the general habitus and sexual desire of their possessor is justifiable." Gross and Meeker[32] have made these very pertinent statements: "The surgical revision of sexual organs or excision of portions thereof, particularly the gonads, has serious legal implications. Apparently, parents have a right to give permission for such undertakings on their children as minors. This does not obviate the fact that the child on attaining the age of 21 years can, if so inclined, bring suit against the surgeon for charges ranging from malpractice to assault and battery, or even mayhem. This disagreeable quirk in the law of the land, which theoretically can lay one open to suit a decade later, in spite of the fact that the legally-responsible parents gave permission at the moment, should not deter physicians and surgeons from handling these unfortunate children with sexual abnormalities in whatever way seems to them and their consultants to be the most suitable and humane."

The views just cited are medical opinions. What do the legal experts say? At present we are unable to cite any legal opinions. A study in cooperation with the Legal Aid Clinic of Duke University has been initiated. A very practical suggestion was made at the initiation of these cooperative medico-legal studies: It might be desirable that states set up commissions or boards on sex assignment or reassignment, comparable to boards of eugenics which authorize sterilization. Such a board or commission could review promptly any problems regarding sex assignment or reassignment and hand down a legal authorization. This would clarify a physician's position, which might be precarious, indeed, if legal action subsequently resulted in a jury trial. It would be a very difficult job to present the medical point of view to a jury.

Several months ago one of our staff tried to determine what would happen when a birth certificate was sent to the Bureau of Vital Statistics with the information "sex unknown." So far, he has had no repercussion from this action. The patient was a newborn with an enlarged phallus and a urogenital sinus defect. Chromatin type was reported negative and, when the study was repeated, chromatin positive. The physician who had delivered the baby

told the parents that the baby was a girl. Consultants believed that the female sex should be assigned because the external genitals did not lend themselves to android reconstruction. The mother took her baby home before studies to rule out congenital adrenal hyperplasia could be done. It was learned subsequently that, shortly after the baby left the hospital, a nurse visited the family and told them that the baby was a boy. Shortly thereafter, the family moved to a distant city.

The record of a patient is given to illustrate some hypothetical or potential medicolegal sequelae: An individual who had been certified and reared as a girl was found to have bilateral abdominal testes and no gynceoid internal genitals when exploratory laparotomy was done at 15 years of age. The parents had given full authorization for necessary surgery. The testes of this individual obviously were secreting estrogens, since the patient had a gynecoid body habitus and stage 3 breasts. The testes were removed. The phallus, being only slightly enlarged, did not require amputation. The patient was given cyclic oral estrogen therapy and obtained an excellent cosmetic result. At no time did the patient have any psychosexual difficulties. She and her parents accepted the explanation that abnormal internal sex organs were removed and that, despite estrogen treatment, she would not menstruate or be able to get pregnant. A very shallow vaginal pouch was developed by sexual activity into a roomy vagina. The patient married and has continued to carry on a satisfactory gynecoid and coital role. From here on we hypothesize. A physician from a distant community, noting the patient's abdominal scar, writes for a report on the nature of her surgery. When this information is secured, the patient learns inadvertently that "she" had been a boy until the testes were removed and that "she" is now a eunuch. Or the husband becomes concerned because his wife does not have periods and cannot become pregnant. Medical investigation is initiated and the information regarding the nature of the wife's previous surgery becomes available. Or someone gratuitously reports from a routine Papanicolaou vaginal smear that the patient has "somatic masculinity" or is chromatin negative. Such hypothetical happenings as these are the seed from which serious medicolegal involvement could arise.

Many other hypothetical patient records could be cited which would unmask the older concept that a patient who had testes should have been certified as male, or that all patients with chromatin-negative status should be designated male. The latter situation could be illustrated well by a morphologically gynecoid individual with Turner's syndrome, who was being properly and adequately treated with estrogens. During a routine examination, vaginal cytology smears were reported "as showing somatic masculinity" or as chromatin negative. Injudiciously supplying the patient with this information well could produce severe psychosexual traumatism.

Reassignment of Sex

When this is necessary, it may be because a physician has decided that the initially assigned sex is less suitable or practical than the sex to be reassigned, or because the parents (or in rare instances, the patient) do not desire the originally assigned sex, either for the reason they do not agree with the surgical methods required to implement this sex, or because they feel that morphological or physiological manifestations indicate that the assigned sex is wrong.

Reassignment Before Eighteen Months of Age.—The gender role is not established by this age. Therefore, sex reassignment is possible. This should

be irrevocable and should be done only after the parents have full understanding and have given written consent. The necessary arrangements should be made for any surgery and/or endocrine therapy to implement the reassigned sex. These plans and those for follow-up should be explained and outlined clearly to the parents. The prognosis for fertility and for menstruation, if the reassigned sex is female, should be given. There is no individual rule for coping with the psychological problems of the parents, relatives, and friends when reassignment of sex is necessary. All important legal documents should be changed: A new birth certificate should be filed (this so often is forgotten) and appropriate changes should be made in insurance policies, wills, and trust agreements.

Reassignment After Gender Role Is Established.—Gender role of most children is well established by 2½ years of age. Reassignment at this time risks serious psychological sequelae and, when it is done, plans should be made for psychiatric follow-up. By middle childhood the gender role is irreversibly established in the majority and a change of sex by edict should not be done.

Voluntary Requests From Individuals for Reassignment of Their Sex.—These are extremely rare even when there are obvious morphological or physiological ambiguities. Under these circumstances, when a change of sex is desired, there has been a defective establishment of the gender role in early years. These requests may be considered favorably if the genitals are amenable to functional, surgical adaptation to the new sex. It is likely, however, that, whether or not sex is reassigned, "such an individual can never establish a thoroughly pervasive and unequivocal gender role."[18]

Psychosexual states, as transvestitism or homosexuality, in morphologically and physiologically normal individuals are not indications for the reassignment of sex. Incidentally, the chromatin type of individuals with transvestitism corresponds with their morphological status.[54]

Summary

The true sex of an individual is not necessarily that which agrees with his or her chromosomes, gonads, hormone production, morphology of the external genitals or that of the internal genitals. After the age of 2½ years, it is definitely the sex of assignment and rearing, fortified by gender role and psychosexual orientation.

Eight clinical types of ambiguities of sexing are classified and synopsized with their chromosomal, morphological, and endocrinological characteristics. These types are reconciled with Jost's theory of the role of the fetal testis in sex differentiation. Sex chromatin data are of ancillary but not primary value in the differentiation of these types.

A practical plan for prompt sex assignment at birth is outlined. This is advisable to avoid psychological trauma to parents and to circumvent gossiping of relatives and acquaintances. Surgery and/or endocrine therapy usually are necessary to implement the assigned sex. Parents should understand this plan to complete the sexual development of their "unfinished" baby. Medical, religious, and medicolegal aspects of the implementation of assigned sex are discussed. The assignment and implementation of a practical sex, before gender role complicates matters, should assure individuals with sexual ambiguities of becoming well-oriented, coitally adequate, if not fertile, adults.

If sex reassignment becomes necessary, it should be done before gender role is established, a new birth certificate should be filed and all pertinent documents, as wills and insurance policies, altered. When sex is reassigned after gender role is established, psychosexual problems arise and rarely, if ever, is a pervasive, convincing, and unequivocal adaptation to the new sex developed.

I am much indebted to Drs. Yancey Culton, Jr., and R. E. McComas of my staff and to my research and editorial secretaries, Mary R. Haddon and Agnes B. Hamblen, for their help in collecting and correlating the materials upon which this paper was based.

References

1. Young, H. H.: Genital Abnormalities, Hermaphroditism and Related Adrenal Diseases, Baltimore, Md., 1937, Williams and Wilkins Company.
2. Barr, M. L., and Bertram, E. G.: Nature **163**: 676, 1949.
3. Wilkins, L., Grumbach, M. M., and Van Wyk, J. J.: J. Clin. Endocrinol. **14**: 1270, 1954.
4. Polani, P. E., Hunter, W. F., and Lennox, B.: Lancet **2**: 120, 1954.
5. Plunkett, E. R., and Barr, M. L.: Anat. Rec. **124**: 348, 1956 (abstract).
6. Bradbury, J. T., Bunge, R. G., and Boccabella, R. A.: J. Clin. Endocrinol. **16**: 689, 1956.
7. Plunkett, E. R., and Barr, M. L.: Lancet **2**: 853, 1956.
8. Grumbach, M. M., Engle, E. T., Blanc, W. A., and Barr, M. L.: J. Clin. Endocrinol. **16**: 923, 1956 (abstract).
9. Jackson, W. P. U., Shapiro, B. G., Uys, C. J., and Hoffenberg, R.: Lancet **2**: 857, 1956.
10. Barr, M. L.: Anat. Rec. **121**: 387, 1955 (abstract).
11. Hamblen, E. C., Carter, F. B., Wortham, J. T., and Zanartu, Juan: Am. J. Obst. & Gynec. **61**: 1, 1951.
12. Money, John: Bull. Johns Hopkins Hosp. **96**: 253, 1955.
13. Hampson, J. G.: Bull. Johns Hopkins Hosp. **96**: 265, 1955.
14. Hampson, J. L., Hampson, J. G., and Money, John: Bull. Johns Hopkins Hosp. **97**: 207, 1955.
15. Money, John, Hampson, J. G., and Hampson, J. L.: Bull. Johns Hopkins Hosp. **97**: 284, 1955.
16. Money, John, Hampson, J. G., and Hampson, J. L.: Bull. Johns Hopkins Hosp. **97**: 301, 1955.
17. Money, John, Hampson, J. G., and Hampson, J. L.: Bull. Johns Hopkins Hosp. **98**: 43, 1956.
18. Hampson, J. G., Money, John, and Hampson, J. L.: J. Clin. Endocrinol. **16**: 547, 1956.
19. Masters, W. H.: In Engle, E. T., and Pincus, Gregory, editors: Hormones and the Aging Process, New York, 1956, Academic Press, Inc.
20. Barr, M. L.: Lancet **1**: 47, 1956.
21. Klebs, E.: Handbuch der pathologischen Anatomie, Berlin, 1876, August Hirschwald.
22. Wilkins, L., Grumbach, M. M., Van Wyk, J. J., Shepard, T. H., and Papadatos, C.: Pediatrics **16**: 287, 1955.
23. Grumbach, M. M., Van Wyk, J. J., and Wilkins, L.: J. Clin. Endocrinol. **15**: 1161, 1955.
24. Wiesner, B. P.: J. Obst. & Gynaec. Brit. Emp. **41**: 867, 1934; **42**: 8, 1935.
25. Jost, A.: Arch. anat. micr. et morphol. expér. **36**: 271, 1947.
26. Jost, A.: Arch. anat. micr. et morphol. expér. **39**: 577, 1950.
27. Jost, A.: In Pincus, G., editor: Recent Progress in Hormone Research, New York, 1953, Academic Press, Inc., vol. 8, p. 379.
28. Lillie, F. R.: J. Exper. Zoöl. **23**: 371, 1917.
29. Gillman, J.: Contrib. Embryol. **32**: 81, 1948.
30. Prunty, F. T. G., McSwiney, R. R., and Clayton, B. E.: J. Clin. Endocrinol. **13**: 1480, 1953.
31. Turner, H. H.: Endocrinology **23**: 566, 1938.
32. Gross, R. E., and Meeker, I. A., Jr.: Pediatrics **16**: 303, 1955.
33. Amelar, R. D.: J. Urol. **76**: 174, 1956.
34. Kozoll, D. D.: Arch. Surg. **45**: 578, 1942.
35. Greene, R., Matthews, D., Hughesdon, P. E., and Howard, Alma: Brit. J. Surg. **40**: 263, 1952.
36. Greene, R., Matthews, D., Hughesdon, P. E., and Howard, Alma: Brit. J. Surg. **41**: 548, 1954.

37. Raynaud, A., and Frilley, M.: Ann. Endocrinol. **8**: 400, 1947.
38. Klinefelter, H. F., Jr., Reifenstein, E. C., Jr., and Albright, F.: J. Clin. Endocrinol. **2**: 615, 1942.
39. Bunge, R. G., and Bradbury, J. T.: J. Clin. Endocrinol. **16**: 1117, 1956.
40. Nelson, W. O.: Acta endocrinol. **23**: 227, 1956.
41. Nelson, W. O.: Personal communication, Nov. 26, 1956.
42. Plunkett, E. R.: Personal communication, Nov. 24, 1956.
43. Brentnall, C. P.: J. Obst. & Gynaec. Brit. Emp. **25**: 235, 1945.
44. Javert, C. T., and Finn, W. F.: Cancer **4**: 60, 1951.
45. Hoffmann, F., Overzier, C., and Uhde, G.: Geburtsh. u. Frauenh. **15**: 1061, 1955 (abstract in J. A. M. A. **160**: 1535, 1956).
46. Overzier, C.: Acta endocrinol. **21**: 97, 1956.
47. Bohle, A., and Hienz, H. A.: Klin. Wchnschr. **34**: 981, 1956 (abstract in J. A. M. A. **163**: 76, 1957).
48. Makowski, E. L., Prem, K. A., and Kaiser, I. H.: Science **123**: 542, 1956.
49. Sachs, L., Serr, D. M., and Danon, M.: Science **123**: 548, 1956.
50. Dewhurst, C. J.: Lancet **1**: 471, 1956.
51. Lowrie, R. G.: Gynecology. Diseases and Minor Surgery, Springfield, Ill., 1952, Charles C Thomas, Publisher.
52. Armstrong, C. N.: Proc. Roy. Soc. Med. **46**: 301, 1953.
53. Wilkins, L.: The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence, Springfield, Ill., 1950, Charles C Thomas, Publisher.
54. Barr, M. L., and Hobbs, G. E.: Lancet **1**: 1109, 1954.

Discussion

DR. DAVID F. WATSON, Greenville, S. C.—Not only is ambiguity of sex of paramount importance to the individual concerned, but the social stigmas may cause involvement of everyone in the family. Extreme caution is indicated before any decision is reached as to assignment of sex initially and even greater caution is indicated when any reassignment of sex is contemplated.

In general, I certainly agree with the substance of Dr. Hamblen's paper. There are a few areas in which I find disagreement, however.

First, Dr. Hamblen has asked us to consider eight different types or groups of intersexualities. I feel that this is spreading a rather rare thing too thin in spots. I see no reason why his types 3 and 4 should not be included in one group because, if they are not, someone will surely find an individual who will not fit exactly into either type and this will necessitate an intermediate type probably called type 3½.

Next, in Dr. Hamblen's Table I, he presents, not his own, but Dr. Wilkins' and Money's collection from the literature of the number of these various types of intersexes. I feel sure that a careful review of the literature such as Dr. Hamblen himself would carry out would disclose a considerably higher incidence of some of these ambiguities.

DR. ROBERT A. ROSS, Chapel Hill, N. C.—The sexual structures normally conform to the chromosomal sex established at the time of conception. There are no reported instances of an individual with XX chromatin pattern who has developed testes nor one with XY chromatin pattern who has developed ovaries. The differentiation of female genital ducts inevitably occurs unless opposed by a functional fetal testis; a functional ovary is not essential.

Anomalies of the sex organs of a newborn should be noted, help from all sources obtained, parents informed, and a course of action established. The family and neighbors are immediately conscious of sex designation, the child itself probably at 18 months or 2 years of age. The all-too-evident compulsion to incise, alter, or remove an organ or a part should be subject to restraint. A "guy named Joe" can be a "gal named Jo." Intelligent direction need not be foolish procrastination and immediate definitive surgery should be based on knowledge, not on expeditious impulse.

DR. HAMBLEN (Closing).—I am glad that Dr. Ross discussed various factors in the ambiguities of sexing. Maternal disease, fetal disease, and fetal accidents are general etiological factors. The genetic effects of nuclear emanations and of cumulative gonadal irradiation, incidental to diagnostic roentgenography, may be factors.

PARENTAL, FETAL, AND ENVIRONMENTAL FACTORS IN PERINATAL MORTALITY*

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PERINATAL deaths constitute one of the major elements of mortality in North Carolina. In 1954 there were 4,500 perinatal deaths compared to 3,700 deaths from malignancy and 2,400 deaths due to all accidental causes. Futhermore, the preventable factors associated with perinatal mortality are largely the responsibility of the obstetrician. Prematurity, birth injury, congenital malformations, asphyxia, atelectasis, maternal toxemia, and erythroblastosis accounted for 86 per cent of all of the neonatal deaths in North Carolina for the year 1954.

Fetal, neonatal, and infant mortality rates in North Carolina are higher than similar rates in most of the other states. A comparison of the fetal, neonatal, and infant mortality rates for North Carolina discloses that the fetal and neonatal rates are considerably higher than the infant mortality rate (Fig. 1). The over-all perinatal mortality rate is higher than the average for the United States (Fig. 2). This difference has been attributed to the high perinatal mortality rate among the non-white group which constitutes approximately one third of the population in North Carolina (Fig. 3). However, a comparison of the perinatal mortality rate for white persons in North Carolina shows that this is also higher than the average perinatal mortality rate among whites in the United States.

Method of Study

The present study was undertaken to learn more about the parental, fetal, and environmental factors which might influence perinatal mortality. The study, initiated in 1954, is being conducted at the North Carolina Memorial Hospital of the University of North Carolina, the Duke University Hospital, and the North Carolina Baptist Hospital associated with the Bowman Gray School of Medicine. The School of Public Health of the University of North Carolina and the North Carolina State Board of Health are cooperating in the study.

A six-page schedule plus a supplement for recording autopsy findings were designed to record the data. The information is obtained from the hospital

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records and by direct interview with the mother. A schedule is completed for all deaths of fetuses of over 20 weeks' gestation and all neonatal deaths occurring in infants born in the participating hospitals. Approximately every fifteenth delivery is selected as a control. The number varies among the three hospitals depending upon the individual hospital perinatal mortality rates.

In the beginning, it was decided to use every tenth patient as a control. It soon became apparent, however, that our controls would outrun the number of deaths, so control cases were adjusted according to the perinatal mortality in each of the contributing hospitals. It is apparent from the tables that the controls actually represented every fifteenth case.

Fig. 1.—Fetal, neonatal, and infant mortality rates for North Carolina at 5 year intervals, 1935 to 1955.

Data

The data in the current report include all the deaths with the appropriate controls between March, 1954 (April for the North Carolina Memorial Hospital), and Jan. 1, 1956, and covers 6,193 total deliveries. As can be seen in Table I there were 279 perinatal deaths, of which 163 were fetal and 116 were neonatal, giving a perinatal mortality of 4.5 per cent.

TABLE I. DISTRIBUTION OF CASES

	FETAL DEATHS	NEONATAL DEATHS	CONTROL INFANTS
Number of cases	163	116	398
White	95	67	278
Non-white	68	49	120

Distribution of the study cases on the basis of weight is presented in Table II. The tremendous impact of prematurity is readily apparent, 70 per cent of the perinatal deaths occurring in the premature category and 60 per cent in the weight group of 2,000 grams or less. There were only 2 infants who weighed less than 2,000 grams in the control group, both in the weight class of 1,500-2,000 grams. The percentage distribution of the controls in the largest two weight

groups is four times as high as the distribution of the perinatal deaths in the same groups. Further weight division in the group weighing over 3,500 grams seems advisable.

The causes of death on the basis of clinical and autopsy findings are listed in Table III. The over-all autopsy rate for the series was 66 per cent.

Socioeconomic Factors.—

It was obvious from a preliminary analysis that socioeconomic factors were of major importance. Race, father's occupation, mother's education, hospital financial classification, and legitimacy were considered in this category. The effect of race on perinatal mortality in North Carolina has been demonstrated

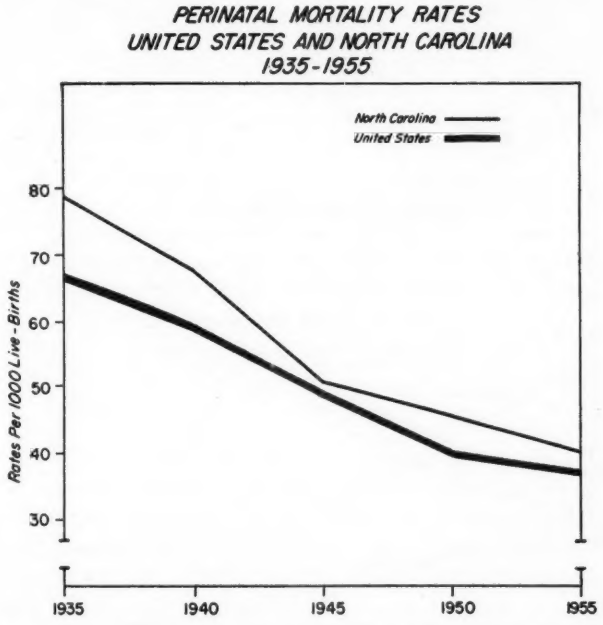

Fig. 2.—Perinatal mortality rates of North Carolina and the United States at 5 year intervals, 1935 to 1955.

(Fig. 3). This difference is also apparent in this study (Table IV). The data in this and subsequent tables are recorded on the basis of percentage distributions. The total number of cases in each group is listed on the top line. Race was recorded in 677 cases, 279 being perinatal deaths and 398 controls. Of the totals, 65 per cent were white and 35 per cent non-white. In the perinatal mortality group 58 per cent were white, whereas in the control group 70 per cent were white. Because of the possibility of other variables these data were

TABLE II. DISTRIBUTION BY WEIGHT*

	FETAL AND NEONATAL DEATHS	CONTROL INFANTS
Total number of cases†	275	398
400-1,000 grams	25.8%	0.0%
1,000-1,500 grams	19.0%	0.0%
1,500-2,000 grams	14.5%	0.5%
2,000-2,500 grams	9.8%	7.8%
2,500-3,000 grams	12.0%	20.3%
3,000-3,500 grams	11.2%	41.4%
3,500 grams plus	7.6%	30.0%

*Significant by chi square test.
†Excludes unknowns.

subjected to covariant analysis for age and parity. Covariant anlysis for socioeconomic factors indicated that race was not a significant factor in perinatal mortality when so adjusted.

TABLE III. CAUSES OF DEATH

CAUSES	FETAL DEATHS	NEONATAL DEATHS	TOTAL
Congenital malformation	15	17	32
Birth injury (asphyxial and mechanical)	50	38	88
Asphyxia and atelectasis	--	19	19
Pneumonia of the newborn	--	2	2
Intrauterine infection	6	1	7
Maternal toxemia	26	--	26
Other maternal disease	16	1	17
Erythroblastosis	5	7	12
Prematurity	15	22	37
Other	2	--	2
Ill-defined and unknown	28	9	37
Total	163	116	279

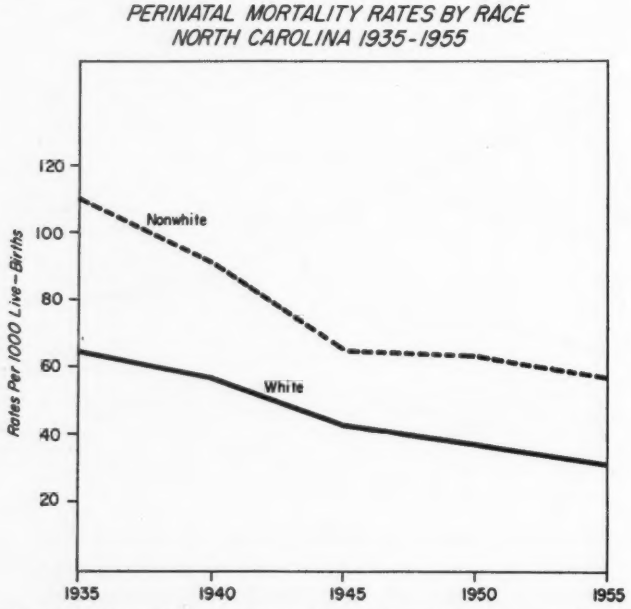

Fig. 3.—Perinatal mortality rates by race in North Carolina at 5 year intervals, 1935 to 1955.

The father's occupation was considered by groups (Table V). Group I consists of professional people, managers, officials, proprietors, and students. Group II consists of clerks, sales workers, craftsmen, foremen, and operators. Group III includes farmers, farm laborers, other laborers, and household workers. The percentage distribution in Group I favors the controls and this is reversed in Group III. Covariant analysis for maternal age, parity, race, and other socioeconomic factors indicated that the father's occupation is highly significant in its relationship to perinatal mortality.

The mother's education, expressed in total years of school attendance, was subjected to a similar analysis (Table VI). These data indicate a more favorable experience for the women who attended school for longer periods of time. The mothers who had 8 years or less schooling accounted for 29.7 per cent of the perinatal deaths and only 16.1 per cent of the controls. The mothers who had more than a high school education showed a reverse distribution. The amount of schooling was considered predominantly a measure of socioeconomic status.

TABLE IV. DISTRIBUTION BY RACE*

	FETAL AND NEONATAL DEATHS	CONTROL INFANTS
Total number of cases	279	398
White	58%	70%
Non-white	42%	30%

*Significant by chi square test.

TABLE V. FATHER'S OCCUPATION*

	FETAL AND NEONATAL DEATHS	CONTROL INFANTS
Total number of cases†	238	368
Group I	18.5%	29.6%
Group II	29.1%	44.4%
Group III	42.4%	26.4%

*Significant by chi square test.
†Excludes unknowns.

TABLE VI. MOTHER'S EDUCATION*

	FETAL AND NEONATAL DEATHS	CONTROL INFANTS
Total number of cases†	151	251
1-8 years	29.7%	16.1%
9-12 years	49.0%	51.4%
13 years plus	21.2%	32.6%

*Significant by chi square test.
†Excludes unknowns.

A study of the hospital financial classification indicated a lower perinatal mortality rate in the private group as compared to the service group. No differences were noted between the married and unmarried groups. This observation might be explained by the fact that a large number of the unmarried mothers in this study were from a well-run Salvation Army Home and received the benefit of excellent prenatal care.

Previous Obstetric History.—

The previous obstetric history of the mother, including the mother's age, birth interval, parity, previous obstetric complications, and previous fetal or neonatal loss, was studied. Consideration of the birth interval, or the length of time between marriage and birth, in primiparas yielded no information of importance. The mother's age, however, appeared to be highly significant (Table VII).

TABLE VII. MOTHER'S AGE*

	FETAL AND NEONATAL DEATHS	CONTROL INFANTS
Total number of cases†	268	397
10-19 years	17.6%	17.6%
20-29 years	47.4%	57.7%
30 years and over	35.1%	24.8%

*Significant by chi square test.
†Excludes unknowns.

In the youngest age group, 10 to 19 years, there was no apparent difference in the percentage distribution. In the next decade the percentage distribution favored the patients in the control group. In women 30 years of age and over, the percentage distribution in the fetal and neonatal group was 35 per cent

which was significantly higher than the percentage distribution of 24.8 per cent in the control group. When age is considered at 5 year intervals the perinatal mortality appears slightly higher in the children of women above 35 years than of those between 30 and 35 years. These data were likewise subjected to covariant analysis for socioeconomic status and parity, but remained highly significant for age in its relation to perinatal mortality. Total parity, on the other hand, when adjusted for age and socioeconomic status, did not appear to be a significant factor in perinatal mortality.

Previous obstetric complications were recorded in 29 per cent of the multiparas (Table VIII). The patients without previous complications made up 75.6 per cent of the control group and only 63.8 per cent of the fetal and neonatal mortality group. A reverse distribution is noted in the group of patients who had a history of previous complications. Covariant analysis for other variables was not done on these data.

TABLE VIII. PREVIOUS OBSTETRIC COMPLICATIONS*

	FETAL AND NEONATAL DEATHS	CONTROL INFANTS
Total number of cases†	185	254
No previous complications	63.8%	75.6%
Previous complications	36.2%	24.4%

*Significant by chi square test.
†Excludes primiparas and unknowns.

Perinatal mortality in a previous pregannecy was studied to ascertain whether or not it had any specific relationship to perinatal mortality with the pregnancy under study (Table IX). The history of a previous perinatal death is associated with a significantly higher percentage distribution in the fetal and neonatal death group than in the control group. Data on previous fetal deaths, adjusted by covariant analysis for age, parity, and socioeconomic index, lost their significance. Similar calculations were not performed on the data relating to previous neonatal deaths.

TABLE IX. PREVIOUS PERINATAL MORTALITY*

	FETAL AND NEONATAL DEATHS	CONTROL INFANTS
Total number of cases†	200	255
No previous perinatal deaths	53.5%	67.0%
One or more previous perinatal deaths	46.5%	33.0%

*Significant by chi square test.
†Excludes unknowns and primiparas.

Prenatal Care.—

The evaluation of prenatal care as a factor in perinatal mortality was surprisingly complicated. Items considered in this category included quantity and source of prenatal care, nutrition, maternal hemoglobin, and iron and vitamin supplementation. Data based on the number and frequency of prenatal visits were inconclusive. When prenatal care was evaluated on the basis of the source of the care, certain differences appeared (Table X).

TABLE X. PRENATAL CARE (TOTAL)*

	FETAL AND NEONATAL DEATHS	CONTROL INFANTS
Total number of cases†	265	390
No care	9.0%	1.8%
Obstetrician and hospital outpatient department	69.5%	89.0%
General practitioner	21.5%	9.2%

*Significant by chi square test.
†Excludes unknowns and 5 cases cared for in Health Department Clinics.

The prenatal care rendered by board obstetricians and that by hospital outpatient department were considered together since the patients in the outpatient department were technically under the supervision of the board obstetricians involved in this study. Examined separately there was a slight difference, with the obstetricians' patients having a slight advantage. In the control group 89 per cent of the patients were given prenatal care by a board obstetrican or in the hospital outpatient department. In contrast only 69.5 per cent of the fetal and neonatal group received prenatal care from these sources. Prenatal care by the general practitioner was given to 9.2 per cent of the patients in the control group. The percentage distribution in the fetal and neonatal group cared for by the general practitioner was considerably higher, 21.5 per cent. There was a similar difference in the groups who received no prenatal care. It should be emphasized that these figures do not represent the over-all practice of the general practitioner. A similar analysis of prenatal care in patients who did not have toxemia or any of the bleeding complications showed a similar but less marked distribution. On the other hand, consideration of only the patients who had toxemia disclosed a similar but exaggerated difference.

Unsuccessful attempts were made to evaluate the patient's nutritional status by recording historically the diet both in childhood and during the pregnancy under study. The mother's prenatal hemoglobin was not significant, at least as far as this study was concerned (Table XI). The percentage distributions in the fetal and neonatal group and the control group are approximately equal at all levels of hemoglobin studied.

TABLE XI. MOTHER'S HEMOGLOBIN

	FETAL AND NEONATAL DEATHS	CONTROL INFANTS
Total number of cases*	248	371
0-8.9 grams	10.5%	9.2%
9-11.9 grams	65.7%	63.3%
12.0 grams and over	23.8%	27.5%

*Excludes unknowns.

Present Puerperal Complications.—

Nonobstetric complications, such as diabetes and heart disease, were encountered infrequently in this study. There were 8 diabetic patients with 8 fetal deaths. Fifteen patients had rheumatic heart disease, 4 with failure. In this group there were 12 perinatal deaths, 8 fetal and 4 neonatal. Both groups were too small for comparison with the control group.

The obstetric complications, toxemia, premature separation of the placenta, placenta previa, and unclassified antepartum bleeding, were found to be highly significant in their relation to perinatal mortality (Table XII). The percentage of cases in the fetal and neonatal group for all of these complications is significantly higher than in the control group. The reverse is true for the patients

who have none of these complications. For example, the percentage distribution for premature separation of the placenta in the fetal and neonatal group is 40 times as high as in the control group. This marked difference may be due to the fact that many of the minor and nontoxic premature separations of the placenta were included in the category of "other antepartum bleeding."

TABLE XII. PRESENT PUERPERAL COMPLICATIONS

	FETAL AND NEONATAL DEATHS	CONTROL INFANTS
Total number of cases	262	387
None	50.4%	88.0%
Toxemia	21.3%	8.3%
Premature separation of placenta	12.6%	0.3%
Placenta previa	2.7%	0.3%
Other antepartum bleeding	13.0%	3.1%

Labor.—

The most significant finding in the items included under the general heading of labor concerns premature rupture of the membranes. This complication occurred in 21.6 per cent of the 636 cases in which information on this point was included on the schedules (Table XIII). Of the control group 17.5 per cent had premature rupture of the membranes, as opposed to 27.8 per cent of the fetal and neonatal group. The length of the latent period associated with premature rupture of the membranes was found to be related to the duration of the pregnancy (Table XIV). The latent period was shorter as term approached. A great deal of the difference in mortality associated with premature rupture of the membranes may be explained on the basis of prematurity (Table XV).

TABLE XIII. PREMATURE RUPTURE OF MEMBRANES*

	FETAL AND NEONATAL DEATHS	CONTROL INFANTS
Total number of cases†	255	381
Rupture during labor	72.2%	82.5%
Rupture before labor	27.8%	17.5%

*Significant by chi square test.
†Excludes unknowns.

TABLE XIV. PREMATURE RUPTURE OF MEMBRANES; LATENT PERIOD RELATED TO PERIOD OF GESTATION

	LESS THEN 27 WEEKS	28-37 WEEKS	38 WEEKS AND OVER
Total number of cases*	30	66	83
Latent period 0-12 hours	20.0%	48.5%	72.3%
12 hours and over	80.0%	51.5%	27.7%

*Excludes unknowns. Includes only cases of premature rupture of the membranes.

TABLE XV. PREMATURE RUPTURE OF MEMBRANES; PERINATAL MORTALITY BY PERIOD OF GESTATION

	FETAL AND NEONATAL DEATHS	CONTROL INFANTS
Total number of cases	95	84
20-27 weeks	31.6%	--
28-37 weeks	52.6%	19.0%
38 weeks and over	15.8%	81.0%

Delivery.—

Perinatal mortality associated with different types of delivery varies considerably as can be seen by comparing the distribution in the fetal and neonatal mortality group against the distribution of the control group (Table XVI).

TABLE XVI. TYPE OF DELIVERY*

	FETAL AND NEONATAL DEATHS	CONTROL INFANTS
Total number of cases†	118	398
Precipitate or unattended	5.9%	0.7%
Spontaneous	50.8%	68.0%
Low forceps	9.4%	21.5%
Midforceps	3.4%	3.5%
Cesarean section	3.4%	1.5%
Version and extraction	2.5%	0.5%
Breech	20.3%	4.3%
Destructive operation	4.2%	--

*Significant by chi square test.
†Excludes infants dead before delivery and unknowns.

Proper evaluation of the type of delivery as a factor in perinatal mortality requires consideration of many factors, such as fetal weight, maternal complications, and fetal abnormalities. A good example of the problems involved can be found in the group of precipitate or unattended deliveries. There were a total of 27 such deliveries. In 17 cases the fetus was known to be dead prior to delivery. In the remaining 10 cases 6 of the infants were in the smallest weight group. Rather than adjust for all of these variables, all breech and all operative deliveries with the exception of low forceps were examined individually. Only 2 perinatal deaths out of the 79 cases reviewed were considered to have been related to the delivery, excluding, of course, the infants delivered by destructive operations.

Summary

The parental, fetal, and environmental factors associated with 279 perinatal deaths and 398 controls have been examined. From the data it is quite evident that socioeconomic factors are of primary importance in perinatal mortality.

The difference in perinatal mortality between the white and non-white groups disappeared when adjusted for socioeconomic factors.

The father's occupation and the mother's education showed significant differences in relation to perinatal mortality even when adjusted for race, age, and parity. The father's occupation and mother's education were considered as indices of the socioeconomic status of the family.

The mother's age was found to be a highly significant factor in perinatal mortality even when adjusted for race, age, and parity.

The technique used in obtaining the data for the present study did not yield reliable information in regard to the nutritional status of the mother.

Birth interval, parity, previous obstetric complications, and previous perinatal mortality did not appear to be significant in relation to perinatal mortality when adjusted for race, age, and parity.

No correlation was noted between the level of the maternal hemoglobin and perinatal mortality.

Certain complications of pregnancy such as toxemia, premature separation of the placenta, placenta previa, and other antepartum bleeding were associated with extremely high perinatal mortality rates.

In this study the type of delivery appeared to have no relationship to perinatal mortality when other variables were considered.

Discussion

LIEUTENANT COLONEL JOHN S. ZELENIK, Fort Benning, Ga.—This paper represents a tremendous amount of work and only those who have been involved in the study, or in a similar study, can completely appreciate the amount of effort that has really gone into its preparation. I speak from some personal experience since at the moment I am in the process of analyzing 485 perinatal deaths associated with 15,154 deliveries at the United States Army Hospital at Forth Benning, Georgia, during the past 6 years. My comments on this paper are based on a partial analysis of these perinatal losses.

I will limit my discussion to two aspects of the problem. The first is premature labor and the second is the socioeconomic factor.

Premature labor is, without a doubt, the most important cause of perinatal death. Fig. 1 shows the distribution of the 485 perinatal deaths by weight. The dark heavy line represents the stillbirths and the dotted line the neonatal deaths. It will be noted that from 2,500 grams upward the neonatal deaths and stillbirths are almost identical lines. (This peak at 3,000 grams represents the mean weight of the 15,154 delivered.) The portion of the chart below 2,500 grams accounts for 72.6 per cent of the perinatal losses but only 7.8 per cent of the total births.

When we compared perinatal losses in brackets of 500 grams we had:

100% loss under 500 grams
97% loss 500 to 1,000 grams
52% loss 1,000 to 1,500 grams
14% loss 1,500 to 2,000 grams
8% loss 2,000 to 2,500 grams
2% loss 2,500 to 3,000 grams
0.74 loss 3,000 to 3,500 grams
0.41 loss 3,500 to 4,500 grams

This proves what we all know, that the bigger the infant, the greater the salvage. We should pay particular attention to this gap between stillbirths and neonatal deaths which occurs in the 500 to 2,500 gram range. It should be noted that in this group there is a striking excess of neonatal deaths over stillbirths. It is apparent that some other mechanism is operating than in term infants since almost twice as many infants are born alive and later die in the premature group than in the term group.

Obviously prematurity is a factor in the death of these infants; however, the essential fact still remains that these infants are born alive and if they could have been kept in utero for a longer period of time might have remained alive. If that dotted line could be brought down to the stillbirth line, either by better postdelivery care, or preferably by preventing the premature birth, a considerable salvage of infants could then be accomplished.

Sharadkar has recommended the ligation of the internal cervical os in patients who have a history of repeated miscarriages after the twentieth week of gestation, and the procedure is being tried in many clinics. Reports coming from Army installations with which I am familiar show about a 75 per cent success where this has been attempted. Obviously the incompetent cervical os is a very small part of this particular problem of perinatal losses, yet it is only by attacking all of these small problems and correcting the many deficiencies that must apply that we can expect to make any progress in this field.

The socioeconomic aspect of the problem has been noted by many in the past. Stewart Taylor at the University of Colorado some years ago pointed out that the incidence of prematurity increased as the economic status of the patients decreased. He based this observation on a comparison of the prematurity rate in three hospitals under his obstetrical supervision.

These were the Fitzsimons Army Hospital, the Colorado General Hospital, and the Denver General Hospital. These hospitals are listed in the order of the decreasing economic status of their patients. The rate of prematurity was lowest at the Fitzsimons Army Hospital and highest at the Denver General Hospital.

After reviewing Dr. Donnelly's paper and noting his breakdown into occupational groups, I felt that we probably had a basis for comparison if I would break our material into three classifications. As our lowest economic group I used the lower half of the enlisted grades; as the middle group the top half of the enlisted grades; and for the top economic group I used the officers. We noticed that there was a distinct differential. Our officer group had an over-all perinatal loss (400 grams and over) of 28 per thousand. Our lowest enlisted ranks had a perinatal loss of 36 per thousand, while the upper enlisted ranks fell roughly in between at 31.4 per thousand. Just what part economics plays in this differential is not clearly understood, but it does seem to me that nutrition must be a factor.

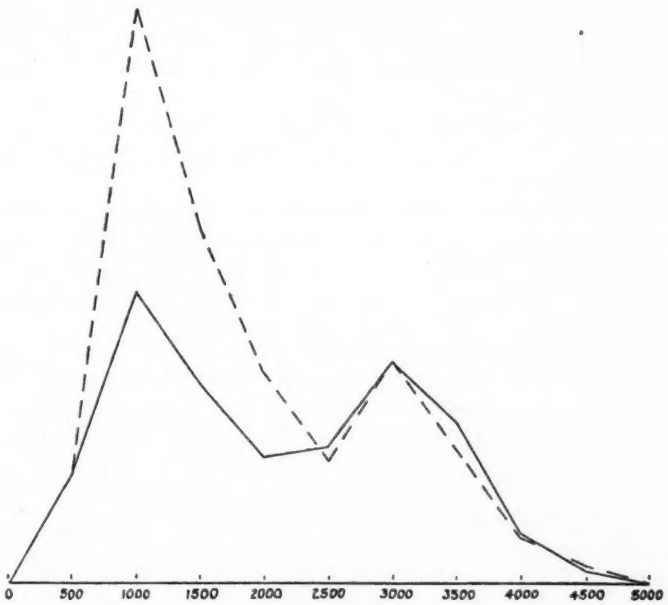

Fig. 1.

You have already seen the results as far as race is concerned. However, when the essayists corrected for occupation the difference seems to disappear. In our population we had 11.5 per cent Negro patients. They had, however, 16.9 per cent of the perinatal losses. Expressed in another way, the perinatal loss rate for our Negro patients was 40.2 per thousand while for our white patients it was 30.6 per thousand. Our Negro patients had over a 30 per cent greater perinatal loss than our white patients. It should be pointed out, that these figures have not been corrected for rank or grade.

DR. ERIC C. SCHELIN, Richmond, Va.—The causes of death in Dr. Donnelly's series closely parallel those in others. It behooves all of us to be alert to the known factors leading to premature delivery, as here again it heads the list. Complete prenatal care, judicious selection of analgesia, if any, together with decreased operative intervention, including induction of labor, constitute a triad which I believe should diminish its incidence and mortality.

In our own study, covering a 10 year period, we had no perinatal loss in patients over 35. This may well be accounted for by improved socioeconomic factors, as we most certainly recognize the potential hazard. We are not averse to a cesarean section in a 40-year-old primigravida with a 10 year period of sterility who develops inertia or who has an abnormal presentation or toxemia.

The higher the hemoglobin and hematocrit, the better we feel, even though they may not affect the baby. Perhaps this is not a statistically valid observation, but it most assuredly seems to us to be an important clinical one. We do not, however, subscribe to the promiscuous use of blood transfusion in maintaining the hemoglobin.

In the bleeding complications at or near term, we feel that both blood and babies are saved by the occasional well-timed cesarean section. I see no glory in 10 transfusions, a bag, and an anoxic baby. In addition, I believe emphasis should again be given to the avoidance of drops in blood pressure in these patients.

Spontaneous premature rupture of the membranes I believe is best managed by bed rest, which is most assuredly an unpleasant ordeal, especially when it occurs weeks before term. It will, however, avoid an appreciable amount of both fetal and maternal morbidity as well as mortality. Only rarely have we used antimicrobial agents.

DR. CHARLES E. FLOWERS, JR., Chapel Hill, N. C.—In the past 5 years much importance has been placed on such factors as erythroblastosis, postmaturity, anesthesia, and analgesia as causes of perinatal mortality. The relatively high perinatal mortality rate in the South is not associated with these minor problems of obstetrics. Ours are still the major issues of obstetrics often associated with limited intelligence, various aspects of Southern culture, and a low per capita income.

Toxemia generally occurs among the medically inarticulate who do not understand the importance of prenatal care. They fail to seek medical advice during pregnancy and, when it is forced upon them, they fail to heed it.

Obstetrical dystocia and hemorrhagic complications of obstetrics are also often related to socioeconomic conditions. When obstetrical complications develop, there must be sufficient intellectual acuity among the patients, the midwives, and the physicians to realize that help is needed. The delay in obtaining definitive medical care is sometimes a factor in maternal mortality but it is often a major factor in perinatal mortality.

Nutrition is often inadequate in the South because of cultural idiosyncrasies and a low per capita income. Foods are prepared by excessive cooking and frying. Salt continues to be the major condiment. It is difficult to prove that poor nutrition is related to prematurity and premature rupture of membranes, but it certainly seems to be an important factor in our perinatal mortality. We have spent millions of dollars on the care of a few premature infants who have a high incidence of morbidity and anatomical abnormalities. It would seem reasonable for the Federal and State Governments to spend more time, thought, and money in the prevention of prematurity.

What can the physicians of the South do to improve these problems? (1) We must work for better education among our patients and encourage them to use the medical knowledge and facilities that are now available. (2) We must improve nutrition by stressing its importance and by improving the eating habits of the low economic group. We should strive for legislation that will allow surplus food commodities to be used to supplement the diets of the indigent prenatal patients. (3) We must try to provide contraceptive advice to the indigent and medically inarticulate. We must continue to study the socioeconomic factors that are related to a high perinatal mortality and possibly formulate some rules concerning socioeconomic indications for sterilization.

DR. DONNELLY (Closing).—In reference to the Rh problem, the paper as read did not have a complete breakdown of the causes of death. There were 12 perinatal deaths due to erythroblastosis, 5 fetal and 7 neonatal deaths.

One other thing about the father's occupation should be mentioned. We considered these people in individual groups. The farm manager, who presumably has a high income and is considered relatively well off financially, had the same high perinatal mortality as the tenant farmer, or nearly so. So the father's occupation involves not only how much money he has in the bank and in his pocket, but certain other factors, one of which is his attitude toward medical care, or custom, or whatever it might be. This is something which requires some education and it is quite possible that we can accomplish this.

THE MANAGEMENT OF TRANSVERSE PRESENTATION*

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THIS study presents an analysis of the methods of treatment of transverse presentation at the University of Virginia Hospital from Jan. 1, 1935, through Dec. 31, 1956. The purpose of presenting this report is to show how a gradual but definite change in management from a policy of vaginal delivery to one of predominant use of cesarean section has favorably affected perinatal mortality in this complication of pregnancy.

Material

During the time covered by the study, a total of 28,092 patients were delivered. One hundred and five patients were admitted with transverse presentation and were delivered. The incidence of transverse presentation was 1 in 268. This incidence is comparable to that reported by others: Garber and Ware,[10] 1 in 419, Novey,[3] 1 in 250, DeLee,[11] 1 in 200, Gareis and Ritzenhaler,[7] 1 in 322.

This study does not include patients with transverse presentation which converted to vertex or breech either spontaneously or by external version prior to the onset of labor or prior to admission. The study is concerned primarily with the management of labor. All of the patients were admitted in labor except 5 who were delivered by cesarean section because of transverse presentation plus some complicating condition. These conditions were: bleeding, placenta previa, previous section, prolapsed arm, rupture of the membranes, and previous myomectomy. Excluded from the study are patients with multiple pregnancies, infants weighing less than 1,500 grams, and oblique presentations.

It is not within the scope of this report to present detailed data on the age distribution, race, parity, or relationship of private to public patients. No detailed study of etiology was undertaken; this has been well presented recently by Stevenson,[4] Harris and Epperson,[5] and others. It is of interest to note that, of the 105 patients, 57 were registered and 48 were unregistered. This is a much higher percentage of unregistered patients than is normal in this hospital but probably is not unusual when compared with the admission of patients with other serious obstetric complications.

Motivation of the Study

In 1951 an informal but detailed review of our experience with transverse presentation, since Jan. 1, 1935, was undertaken. The important information

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found is recorded in detail in Tables I, II, and III, but of greatest interest to us was the perinatal mortality of 58.3 per cent in the group delivered vaginally and 13.8 per cent in the group delivered by cesarean section. Correcting these mortality figures (only for fetuses dead on admission of the mother to the hospital) did not appreciably alter this overwhelming ratio. A careful review of the literature at that time indicated fetal mortality rates of similar or greater magnitude. These facts substantiated our belief that improvement in perinatal mortality was a definite necessity and that more liberal use of cesarean section might be a method of accomplishing this end.

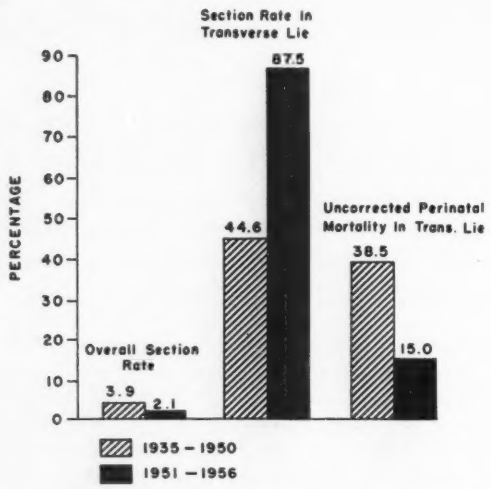

Fig. 1.—The relation of perinatal mortality to section rate in transverse presentation and the over-all section rate.

Since Jan. 1, 1951, the treatment of each patient admitted in labor with transverse presentation has been considered individually and no routine treatment has been established for this complication but, as is seen in Fig. 1, a definite increase in the use of cesarean section has been maintained. The entire group of 105 patients is therefore presented in two series. Series A contains all patients (65) delivered from Jan. 1, 1935, to Jan. 1, 1951. Series B contains all patients delivered between Jan. 1, 1951, and Jan. 1, 1957. The incidence in Series A is 1 in 269 and in Series B 1 in 265.

Maternal Mortality

There was one maternal death in the combined series of 105 patients, an incidence of 0.95 per cent. This study does not show any significant difference in maternal mortality in Series A and B. The only maternal death in Series A occurred as the result of rupture of the uterus and mismanagement following internal podalic version and extraction. The operator disregarded a fundamental obstetrical principle in failing to explore the uterus and accordingly did not recognize rupture. The patient developed a hematoma of the broad ligament and died 21 days after delivery of hemorrhage and infection. This maternal death occurred in 1937. There were no maternal deaths in Series B.

Perinatal Mortality

Table I shows the perinatal mortality in both series, including premature infants weighing over 1,500 grams. In comparing methods of delivery, it is

proper to correct the perinatal mortality for fetuses already dead on admission of the mother because neither method of delivery could have improved the mortality rate. On this basis, the corrected perinatal mortality for all vaginal deliveries is 17.0 per cent and for all cesarean deliveries is 4.7 per cent.

TABLE I. PERINATAL MORTALITY IN CASES OF TRANSVERSE PRESENTATION

METHOD OF DELIVERY	SERIES A, 1935-1950						SERIES B, 1951-1956					
	NO. OF PATIENTS		DEATHS		PERINATAL MORTALITY		NO. OF PATIENTS		DEATHS		PERINATAL MORTALITY	
	NO.	CORRECTED*	NO.	CORRECTED*	%	CORRECTED*	NO.	CORRECTED*	NO.	CORRECTED*	%	CORRECTED*
Vaginal	36	21	21	6	58.3	28.5	5	4	2	1	40.0	25.0
Abdominal	29	29	4	4	13.8	13.8	35	32	4	1	11.4	3.2
Total	65	50	25	10	38.4	20.0	40	36	6	2	15.0	5.6

*Corrected only for intrauterine death of fetus at time of admission of patient to hospital.

The exact methods of delivery in the two series are recorded in Tables II and III.

TABLE II. CESAREAN SECTION: METHODS AND PERINATAL MORTALITY

METHOD OF DELIVERY	SERIES A, 1935-1950			SERIES B, 1951-1956		
	NO. OF PATIENTS	DEADBORN	NEONATAL DEATHS	NO. OF PATIENTS	DEADBORN*	NEONATAL DEATHS
Classical	14	0	1	14	1	0
Laparotrachelotomy	10	0	2	13	0	0
Cesarean hysterectomy	4	0	1	7	3	0
Extraperitoneal	1	0	0	1	0	0

*Of the 4 deadborn in series B delivered abdominally, 3 were dead on admission and the placenta of the fourth showed massive premature separation.

TABLE III. VAGINAL DELIVERY: METHODS AND PERINATAL MORTALITY

METHOD OF DELIVERY	SERIES A, 1935-1950			SERIES B, 1951-1956		
	NO. OF PATIENTS	DEADBORN	NEONATAL DEATHS	NO. OF PATIENTS	DEADBORN	NEONATAL DEATHS
Internal podalic version	20	5	2	5	1	1
Embryotomy	5	5	0	0	0	0
Braxton Hicks version	3	2	0	0	0	0
Conduplicato corpore	3	3	0	0	0	0
External version	2	1	1	0	0	0
Voorhees bag and version	2	0	1	0	0	0
Evolution of Douglas	1	0	1	0	0	0
Total	36	16	5	5	1	1

Prolapse of Fetal Parts

The incidence of prolapse of arm, cord, or both in Series A was 20 per cent. The perinatal mortality when prolapse occurred was 69.2 per cent. In Series B the incidence of prolapse of arm, cord, or both was 35.0 per cent and the corresponding perinatal mortality was 35.7 per cent, showing a significant reduction in mortality in this group delivered predominantly by cesarean section. Furthermore, in Series B, the perinatal mortality, with prolapse, was nearly 10 times the mortality when a fetal part did not prolapse.

Methods of Management and Their Complications

There are maternal and fetal complications of transverse presentation, the causes of which cannot always be controlled. Antepartal bleeding with placenta previa, neglect of the laboring patient to seek proper medical care with resulting rupture of the uterus or overwhelming intrauterine infection, rupture of the membranes prior to admission with prolapse of the cord and fetal death, these and other complications may have serious consequences before the patient is seen. Of special interest to us in reviewing the records of these 105 patients and in carefully reading the current literature on transverse presentation is the frequency with which serious, even fatal, complications are caused by the method of management instituted after admission. We wish to consider these methods and their potential sequelae in detail.

External Version After Onset of Labor.—We agree that external version should be done in the patient with transverse presentation, near term but not in labor, provided that placenta previa has been ruled out by x-ray, that the membranes are intact, and that there is no obstructive pelvic lesion.

Our experience with external version after the onset of labor is limited but has made us dubious of its value. Actually, the number of patients who underwent this procedure was reduced because of the fact that version should not be done if the membranes are ruptured, and membranes had ruptured prior to admission in 37.1 per cent of the 105 patients. External version following the onset of labor was done in 2 patients in Series A. In one patient rupture of the uterus occurred and the other patient delivered a deadborn child which had been viable on admission.

Mangone and Kane[9] report rupture of uterus following external version in labor in one patient and do not indicate that the procedure was done in any other of their 86 patients. Gareis and Ritzenhaler[7] reported a 17.6 per cent fetal mortality in patients so managed. This, however, was the lowest fetal mortality in the patients delivered vaginally. Garber and Ware[10] reported a fetal death in their one patient managed by external version during labor. Eastman[6] approves the procedure in multiparas in very early labor and states that the procedure may occasionally be rewarded with success. Our opinion, based on our experience, is that, if the presentation is truly transverse, not oblique, and the patient is in active labor, the dangers of external version to mother and child outweigh the advantage of occasional success. Certainly if the procedure is attempted the membranes should be intact, the labor very early, the uterus not tetanic, the pelvis adequate, the placenta located, and facilities for laparotomy immediately available.

Spontaneous Delivery.—This method of management was followed in 4 patients. All were admitted in advanced labor. All babies were deadborn. Eventual spontaneous delivery by conduplicato corpore or spontaneous evolution should never be anticipated in patients in early labor. Most such patients will progress to the state of neglect with rupture of the uterus or severe uterine infection. If a patient is admitted late in labor and spontaneous delivery is permitted, the uterus should be explored for possible rupture immediately after delivery.

Internal Version.—Internal podalic and Braxton Hicks version in our combined series carries a fetal mortality of 39.3 per cent which, corrected for babies dead on admission of the mother to the hospital, is 16.7 per cent. Our one maternal death followed internal podalic version, as previously mentioned. In one other patient, who survived, rupture of the uterus followed this procedure. In the 6 maternal deaths in 65 patients reported by Garber and Ware,[10] the method of delivery was internal podalic version and extraction

in 4 patients and Braxton Hicks version and extraction in one patient. Mangone and Kane,[9] in a series of 86 patients, reported 41 delivered by internal version and 16 by Braxton Hicks version. There were no maternal deaths. Two uteri were ruptured, one in each method of delivery by internal version. Harris and Epperson,[5] in a series of 131 patients, reported 54 internal versions of some type. One maternal death, following rupture of the uterus, occurred in this group.

In all of the recent series on transverse presentation, the fetal mortality following the internal version methods is very high, even when corrected for babies dead on admission of the mother. Harris and Epperson reported a corrected perinatal mortality of 39.1 per cent. In Mangone and Kane's series the uncorrected perinatal mortality for internal version is 43.8 per cent and for Braxton Hicks version 62.5 per cent. Garber and Ware reported a perinatal mortality of 87.9 per cent following internal version and 90.9 per cent in Braxton Hicks version.

We have been opposed, during the past 6 years, to allowing the patient who is admitted in labor with transverse presentation to progress with the hope that full dilatation will be reached so that internal podalic version may be done. Prolapse of the cord, a fetal part, or both in over one fourth of all our patients, with a perinatal mortality of 51.8 per cent when such prolapse occurs, indicates that this method of management constitutes a real danger to the fetus. The risk of this and rupture of the uterus, in our experience, is much greater than the risk incurred in cesarean section. In recent years we have used internal podalic version only in patients who have been admitted with intact membranes, and complete or nearly complete dilatation of the cervix, and with small infants; we do not expect to use it in any other group. We have not employed Braxton Hicks version in over six years.

Voorhees Bags.—There are few references to the use of Voorhees bags in recent reports on transverse presentation. Gareis and Ritzenhaler, Garber and Ware, and Mangone and Kane, reporting a combined total of 313 cases, do not mention the procedure. Harris and Epperson, reporting on the use of bags in 18 of 131 patients, indicate a corrected fetal mortality of 20 per cent. The bag failed to produce satisfactory dilatation in 5 of the 18 patients. We have not used Voorhees bags in transverse presentation during the past 6 years. They were used twice in Series A. One child survived and one died. Aside from frequently being a poor dilator of the cervix and causing intrauterine infection, the bag, at the time of insertion, may actually rupture the membranes whose integrity one is trying so hard to maintain, or cause prolapse of the cord.

Cesarean Section.—A plea for more frequent use of cesarean section, as a means of lowering perinatal and maternal mortality, has been made by most of the authors in recent reports of transverse presentation. Harris and Epperson reported 3 maternal deaths after section. Nevertheless, they also urge a more frequent use of section based on their over-all experience. The perinatal and maternal mortality rates in our Series B, so much lower than those reported in any series in which vaginal deliveries predominate or in our own Series A, indicate this to be a rational suggestion.

In Series B our incidence of cesarean section is 87.5 per cent. We have great respect for the maternal and fetal hazards of cesarean section and wish to point out that the percentage of all cesarean sections, public and private, initial and repeat, during the years covered in Series B, is 2.1 per cent. As shown in Fig. 1, our increased use of cesarean section in this complication has not been reflected in a relaxed approach to cesarean section in general. In fact, the cesarean section rate for all patients during the time covered by

Series B is considerably lower than the rate in Series A. There were no maternal deaths in Series B and the uncorrected perinatal mortality rate of 15 per cent for all deliveries in this series is among the lowest reported.

Management of the Patient

Early recognition of the abnormal presentation is important regardless of the type of delivery but is essential if cesarean section is to be employed as a method of decreasing perinatal mortality. One of the reasons for failure to recognize transverse presentation is a blind reliance on the fetal position at the last prenatal visit. Failure to recognize transverse presentation, at the time of admission and during labor, probably resulted in the death of all of the infants who died in Series B who were alive on admission of the mother to the hospital. In this regard, it is of considerable interest to note that of the 22 registered patients in Series B, the position recorded at the last prenatal visit was vertex in 11 patients and transverse in only 5. The others were breech, oblique, or unrecorded. When the diagnosis of transverse presentation is made or suspected, or should there be any question of presentation, x-ray of the abdomen should be done to locate the infant precisely and, as Stevenson and others have suggested, attempt should be made to locate the placenta by placentography. When the diagnosis is made prior to labor, external version should be performed, as noted previously.

Patients with transverse presentation are initially seen in labor with many varieties of circumstances of fetal presentation, fetal heart tone, cervical dilatation, rupture or unrupture of membranes, neglect, and maternal exhaustion. In the management of each patient, all such circumstances must be carefully considered and the patient treated accordingly. There should be no routine treatment but it should be clear from this analysis that, in our opinion, cesarean section should be given a strong consideration in the treatment of most patients.

Two thirds of our patients, when first seen in labor, had intact membranes. The decision to be made in this group is whether to allow labor to progress, in the hope that the membranes will not rupture and the cord not prolapse, or to perform a cesarean section early in labor. The weighing of risks, both fetal and maternal, appears to us from our analysis to favor section in labor, as soon as possible after the diagnosis of transverse presentation is made. Our view is that the parity of the patient should not be considered in this decision. If the membranes are ruptured, decision in favor of section seems to us even more necessary, the patient being carefully watched for occult prolapse of the cord while the operating room is being prepared.

There is room for personal choice in the type of cesarean section used. In general, we have come to prefer the classical section over laparotrachelotomy, especially if the membranes are ruptured or a contraction ring is present, because of the difficulty in reaching either fetal pole through the low-flap incision under these conditions. If the membranes are not ruptured, laparotrachelotomy usually may be done. The chief objection to the transverse lower segment incision is that frequently it must be extended or a T incision made, in order to deliver the child through a contraction ring. This results in a potentially weak, cornered scar.

Obstetric teaching from the time of von Braun dictates that cesarean section should not be done if the baby is dead. We believe that a compromise with this dictum must, at times, be reached when the patient is admitted with neglected transverse lie. Here the child is dead, a fetal part has usually prolapsed, the uterus is tightly contracted, the lower segment thin, and a pathological contraction ring is usually present.

It is our opinion that internal podalic version has no place under these conditions. In such cases we have performed cesarean hysterectomy upon multiparas in whom preservation of reproduction is of relative importance. In patients for whom preservation of the childbearing function is of paramount importance, extraperitoneal section may be attempted, and was performed successfully twice in our combined series. Because of the contraction ring almost invariably present in such patients, extraperitoneal section will rarely be successful, however, and in recent years we have performed classical section with massive antibiotic coverage. We believe this method to be less hazardous to the mother than internal podalic version in the presence of neglect, a dead baby, and a contraction ring. There is room for personal judgment based on the operator's experience in the choice of section.

When patients are admitted at or near full dilatation, with a normally laboring or relaxed uterus and a dead baby with prolapsed arm, embryotomy may occasionally be performed after full dilatation. This was done in 5 cases in Series A. In each instance the prolapsed arm was disarticulated at the shoulder and internal version and extraction then done. We wish to emphasize again that cases for embryotomy must be carefully selected and where the elements of neglect, already listed, are present, delivery from above should receive strong consideration.

The chief objection to increased use of cesarean section appears to us to be the anticipation of postoperative complications in the section group. Except for one patient with wound dehiscence in Series B, there were no serious postoperative complications in that series. In Series A, the postpartal morbidity, according to the standard established by the American Joint Committee on Maternal Welfare for patients delivered vaginally, was 54 per cent and by cesarean section 51.5 per cent. In Series B the morbidity for the few patients delivered vaginally was 0 and by cesarean section 30 per cent.

Summary and Conclusions

1. The records of 105 patients admitted with transverse presentation are analyzed in regard to the method of delivery. One hundred patients were admitted in labor, 5 were admitted not in labor but with transverse presentation plus some secondary indication for cesarean section.

2. The natural hazards of transverse presentation to the mother and infant are recorded, as well as the dangers produced by the available methods of delivery in transverse presentation.

3. There was one maternal death, in 1937, resulting from rupture of the uterus, hemorrhage, and infection, following internal podalic version.

4. Perinatal mortality by the various methods of delivery is shown.

5. It is recognized that in this complication, as in all others, the treatment of each patient must be carefully individualized. Our analysis shows, however, that whereas, in vaginal delivery, the perinatal mortality in this, as well as in other series, is unnecessarily high, the perinatal mortality in infants delivered by cesarean section is relatively very low.

References

1. Eastman, N. J.: Am. J. Obst. & Gynec. **24**: 40, 1932.
2. Johnson, C. M.: Am. J. Obst. & Gynec. **57**: 765, 1949.
3. Novey, M. A., and Schneider, M. M.: Am. J. Obst. & Gynec. **41**: 253, 1941.
4. Stevenson, G. S.: Am. J. Obst. & Gynec. **58**: 432, 1949.
5. Harris, Bruce A., Jr., and Epperson, J. W. W.: Am. J. Obst. & Gynec. **59**: 1105, 1950.

6. Eastman, Nicholson J.: Williams Obstetrics, ed. 11, New York, 1950, Appleton-Century-Crofts Company, Inc.
7. Gareis, L. C., and Ritzenhaler, J. C.: AM. J. OBST. & GYNEC. 63: 583, 1952.
8. Stevenson, C. S.: AM. J. OBST. & GYNEC. 62: 488, 1951.
9. Mangone, E., and Kane, W. M.: AM. J. OBST. & GYNEC. 69: 742, 1955.
10. Garber, E. C., Jr., and Ware, H. H., Jr.: AM. J. OBST. & GYNEC. 61: 62, 1951.
11. DeLee, J. B., and Greenhill, J. P.: The Principles and Practice of Obstetrics, ed. 9, Philadelphia, 1947, W. B. Saunders Company, p. 573.

Discussion

DR. WILLARD C. HEARIN, JR., Greenville, S. C.—Cesarean section is not the formidable procedure it was 20 years ago. I believe that this paper shows that it is a far safer procedure for both the mother and the baby than is version and extraction. There was a time when version possibly was safer for the mother (if not the baby) than section but that time has passed. We need only to look at the number of reported ruptured uteri to appreciate this fact. We all hate to perform a cesarean section on a patient with a known dead baby but we must realize that a dead baby is not an absolute indication for vaginal delivery. We must also consider the possible danger to the mother that may be incurred in a traumatic delivery.

I would like to emphasize that any patient with a known transverse presentation which is uncorrected prior to labor should be warned to report to the hospital immediately upon the first sign of labor or rupture of the membranes. Patients with the diagnosis of transverse presentation on admission must be carefully watched for rupture of the membranes and subsequent prolapse of the cord or fetal part while preparations are being made for cesarean section. It is best to have an emergency cesarean section set available in the delivery suite. This can be a lifesaving factor in sudden obstetrical emergencies.

DR. W. R. WOOD, Greensboro, N. C.—I regret that oblique presentation has been omitted from this study because I believe that it is just another step or stage in the evolution of transverse lie, or actually an incomplete one. Certainly, with a patient in labor and with an oblique presentation with a breech in the lead, we are not going to worry about a patient with the average pelvis, except for the ever present danger of prolapsed cord; however, with a head in the lead, we have to think of such problems as face, brow, shoulder, and prolapsed cord. Certainly, many of the cases of impacted shoulders, prolapsed arms, etc., late in labor, started out as a transverse lie.

A few exceptions to the rule that cesarean section is the proper management for transverse lie include a previable fetus and the rare instance of a multipara with a large pelvis, intact membranes, and complete cervical dilatation, allowing for an easy internal podalic version. I am always loathe to perform cesarean section for a known dead baby and have never been faced with the decision in transverse lie, at or near term, but the alternative of a destructive operation on the fetus, and the high incidence of ruptured uterus with internal version leaves one with but little choice.

In the hands of others, external version seems to be a panacea, but in mine the procedure has been a total waste of time. I have a pretty strong conviction that some of the staunch advocates of this procedure who report such good results at from 30 to 36 weeks would do just about as well with a similar group left alone. I agree wholeheartedly with the essayist that it has no place after the onset of labor.

DR. L. A. CALKINS, Kansas City, Kan.—It so happens that we have also, very belatedly reviewed our experience with this presentation and we were amazed to learn two things, both of which have been alluded to this morning. The first is the perfectly horrible perinatal mortality. We have had several papers in the last 15 years on transverse lie, but only a few of these came near telling the whole story about the problem. The second thing I would like to re-emphasize is the very high percentage of cases of placenta previa associated with transverse presentation. In every article I read there was an estimated 10

per cent of placenta previa. A diagnosis of transverse lie indicates an immediate analysis of the situation to see whether placenta previa may not also be present. We do not do external versions during labor, or before labor begins, until we have ruled out placenta previa.

One of your honorary members, Dr. Nicholson Eastman, started a trend with his paper in 1942—a trend away from version toward cesarean section. Other people since that time have continued to feel that they should do more cesarean sections.

I do feel that there is still a place for version in certain situations. I think we cannot advise cesarean section when we are dealing with a very small baby. The added risk to the mother of cesarean section is not justified and the risk of ruptured uterus is less than with a large baby. I think the patient who comes into the hospital in labor at or near full dilatation, with the baby still alive, should, perhaps, have a version. And, third, I do not believe cesarean section is justified when we find a transverse lie in the second twin.

Transverse presentation is very rare in a primigravid woman. It occurs less than once in 1,000 patients. It is approximately five times as great in the multigravid patient, roughly 5 in 1,000. And it is particularly great in the grand multipara. All of us know that the grand multipara's uterus is much more easy to rupture than that of the woman who has had only one or two babies. I think that must be a factor in our decision. Here is a condition, then, for which we are not called upon to create obstetric cripples by doing many cesarean sections in young women. We need do it usually only in a much older patient who has many fewer future pregnancies to face.

DR. WILSON (Closing).—I do not think it makes a great deal of difference which type of section one does. You will recall from Table II that there were approximately an equal number of classical and low-flap sections. In general, we use the low-flap section when the membranes are intact but prefer the classical when there has been a state of neglect or when the uterus is tightly contracted around the fetus.

There may be extreme difficulty in making an incision in the part of the uterus which contains a pathological contraction ring, which may be from 3 to 6 cm. in thickness, and then inserting the hand into the uterus to remove the child. Even if a ring is not present, it is sometimes necessary, when the low transverse incision is made, to extend the incision cephalad which weakens the scar.

I would object to doing cesarean sections more or less routinely on patients who have an oblique presentation, as Dr. Wood has suggested. Most of these will convert to one pole or the other after labor has begun. If it becomes obvious, as labor progresses, that the presentation has changed from oblique to transverse, I certainly would agree that cesarean section is the better approach.

URETERAL INJURY IN PELVIC SURGERY: REPORT OF A CASE*

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PELVIC surgery is frequently associated with accidental injury to the ureter and bladder. If the possibility of urinary tract injury is constantly kept in mind, the diagnosis of surgical injury is usually not difficult to make. When the diagnosis of injury to the ureter is made at the time of operation, its immediate repair by end-to-end anastomosis over a ureteral catheter and the insertion of a retroperitoneal drain should permit an excellent prognosis for normal kidney function. Reimplantation of the ureter into the bladder may be necessary if the distal ureteral segment is not sufficiently long, or if a considerable portion of the distal segment has been destroyed.

B. E. D., a 33-year-old white married woman, para ii, gravida iii, had last been seen on Jan. 4, 1955, at the time of her six weeks post partum examination. At that time her pelvic examination was essentially normal except for slight enlargement of the uterus. She was first seen for this illness on Dec. 13, 1955, at which time she stated that she had noticed a gradual increase in the girth of the lower abdomen during the last two to three months, associated with some abdominal pain. The menstrual periods had been regular and normal. The abdomen was distended by a soft, cystic-feeling mass rising midway between the symphysis pubis and the umbilicus. The pelvic examination showed a soft, cystic mass completely filling the pelvis, approximately the size of a 4½ to 5 months' gestation. A tentative diagnosis of left ovarian cyst was made. A flat plate of the abdomen at this time showed a soft-tissue mass extending out of the pelvis up to the lower border of the fourth lumbar vertebra. A rabbit test for pregnancy was negative.

A laparotomy was carried out on Jan. 3, 1956, at which time the vagina was prepared and a Robinson retention catheter placed in the bladder. A large intraligamentous cystic mass was found arising from the left ovary, filling the pelvis, and extending almost to the level of the umbilicus. The right adnexa and the uterus were normal. Dissection was started at the superior aspect of the left broad ligament. The posterior leaf of the broad ligament was dissected free, and the mass was rotated anteriorly so that it could be delivered through the abdominal incision. At this point, high in the pelvis a structure was found which seemed to go directly into the capsule of the cystic mass. This structure was palpated, and it had a definite pulsation. After careful inspection it was felt that this was a blood vessel and that it would have to be clamped and cut in order to release the mass so the cyst could be removed unruptured. The possibility that this was the ureter was considered to be remote. The structure was then clamped and cut, and it was immediately recognized that the ureter had been completely severed. The clamp was removed, and urine could be seen to escape from the cut proximal end. The cystic mass and left Fallopian tube were then removed unruptured without further difficulty.

Inspection of the lateral pelvic wall showed that the ureter had been completely severed approximately 2½ inches above the bladder. Fig. 1 shows the technique used in the

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ureteroureterostomy. A No. 6 ureteral catheter was passed up to the pelvis of the left kidney and the distal end threaded down through the lower segment of the ureter into the bladder. The cut ends were then brought together over the catheter with four interrupted vertical mattress sutures of No. 0000 chromic catgut on an atraumatic needle. These sutures were placed entirely within the adventitia of the ureter. A Penrose drain was then placed extraperitoneally down to the site of the ureteral injury. The drain was brought out through the lower third of the abdominal incision. The lateral pelvic wall was completely reperitonealized, and the abdomen was closed.

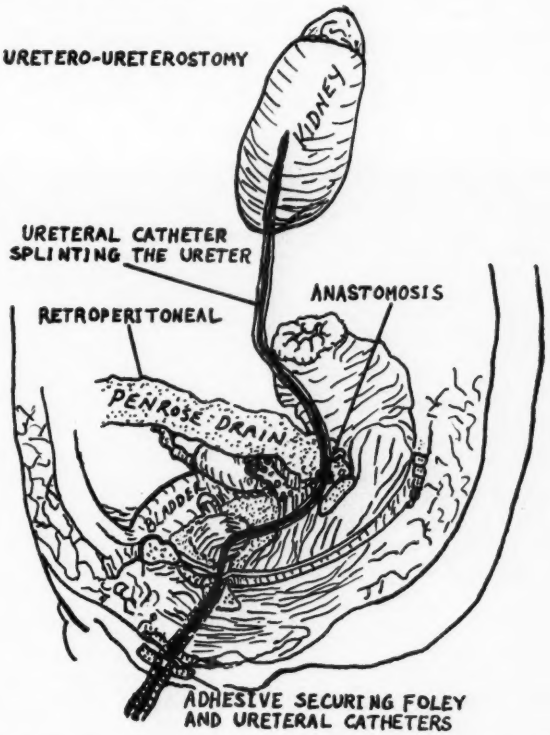

Fig. 1.—Diagram of the ureteroureterostomy, showing the end-to-end anastomosis of the ureter with a ureteral catheter used as a splint, and providing for urinary extravasation by the use of a retroperitoneal drain.

The Robinson catheter was replaced by a No. 18 5 c.c. Foley bag catheter, and the ureteral catheter was taped to the Foley catheter just outside the introitus. Both the Foley catheter and the ureteral catheter were connected for continuous drainage, and both began to show grossly bloody urine immediately. The immediate postoperative course was uneventful. In addition to the routine postoperative orders, the patient was placed on antibiotics.

Fig. 2 shows the 15 minute intravenous pyelogram taken on the second postoperative day. There is delayed kidney function on the left with minimal hydronephrosis. The Penrose drain became dry by the sixth postoperative day, and it was removed, following which the abdomen healed without any drainage from the abdominal wound. The temperature was entirely normal for the entire postoperative stay except for two rises on the eighth and ninth postoperative days to 100.4 and 100.6° F., respectively. The patient developed a mild intestinal upset at this time with diarrhea. Negative pressure was occasionally applied to the ureteral catheter, and it was irrigated with a very small amount of sterile saline on two occasions. The patient was kept flat in bed until both the ureteral and the urethral catheters were removed on the fourteenth postoperative day. She was discharged asymptomatic on the fifteenth postoperative day.

When next seen in the office on Feb. 3, 1956, she was asymptomatic, and the pelvic examination was essentially normal. Intravenous pyelograms taken one month postoperatively showed delayed function of the left kidney with a definite hydronephrosis. Approximately 2 months postoperatively, intravenous pyelograms showed an essentially normal upper urinary tract bilaterally. The patient was last seen on Nov. 8, 1956, at which time she was entirely asymptomatic, and the pelvis was essentially normal. At this time she had a cystoscopy, and a No. 5 ureteral catheter was passed rather easily up the left ureter with no sense of obstruction. The urine was entirely normal at this time. Fig. 3 shows the retrograde pyeloureterogram done on Nov. 8, 1956, approximately ten months postoperatively. It shows a perfectly normal left kidney pelvis and left ureter.

The pathological interpretation of the tissue removed was "normal fallopian tube; unruptured pseudomucinous cystadenoma of the ovary, measuring 16 by 20 by 9 cm."

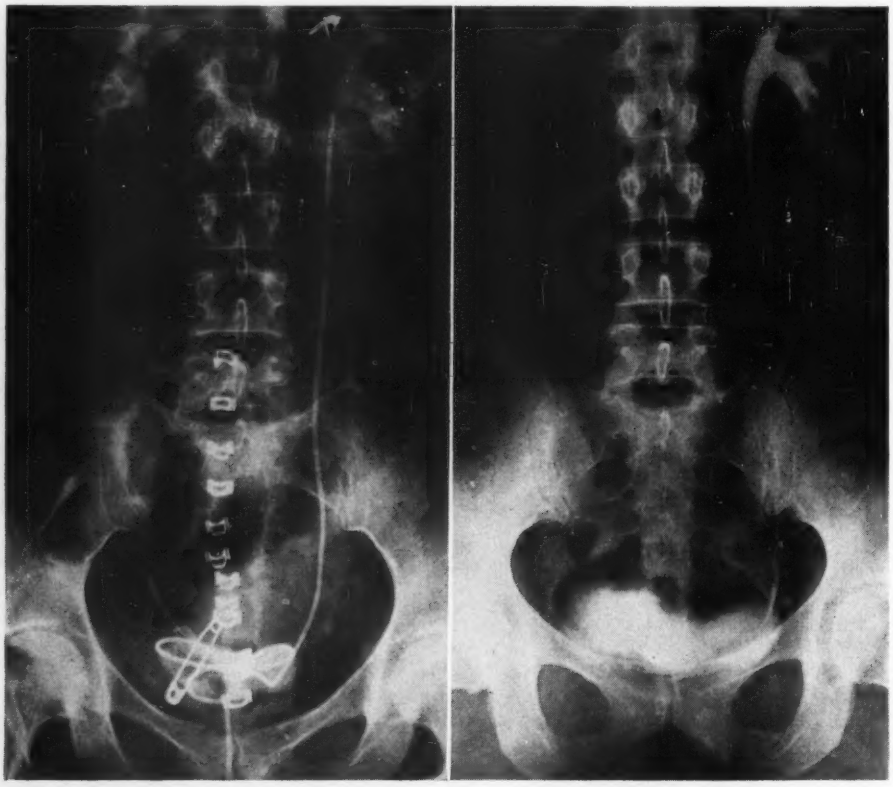

Fig. 2. Fig. 3.

Fig. 2.—Fifteen-minute intravenous pyelogram taken Jan. 5, 1956, the second post-operative day, showing delayed kidney function on the left with minimal hydronephrosis.

Fig. 3.—Retrograde pyeloureterogram with the ureteral catheter removed, taken on Nov. 8, 1956, approximately 10 months postoperatively, showing a perfectly normal left kidney pelvis and left ureter.

Comment

The medicolegal aspect of accidental urinary tract injury is a very important problem. It is my feeling that the patient and her husband or family should be given a full account of the complication as soon as it is practical to do so. They should be told that the complication will probably prolong the convalescence somewhat, but that the complete return to normal kidney function

can be expected. This case shows the return to normal function of the left kidney after the left ureter had been accidentally severed at the time of surgical removal of an intraligamentous pseudomucinous cystadenoma of the left ovary. The technique used in the immediate ureteroureterostomy has been outlined.

References

1. Benson, Ralph C., and Hinman, Frank, Jr.: Am. J. Obst. & Gynec. **70**: 467, 1955.
2. Muluf, N. S. R., and Halpert, Bela: Am. J. Obst. & Gynec. **72**: 377, 1956.
3. O'Conner, Vincent J.: J. A. M. A. **162**: 1201, 1956.
4. Baird, H. Haynes, and Justis, Homer R.: J. A. M. A. **162**: 1357, 1956.

COMBINED TUBAL AND INTRAUTERINE PREGNANCY*

Report of a Case

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THE simultaneous presence of intrauterine and extrauterine pregnancies in the same patient is nearly always described in the literature as a rare condition. In 1952 Zarou and Sy[1] found 415 published cases of this condition. Two reviews in 1956 by Viviano[2] and by Vasicka and Grable[3] brought this total to 444. There are 4 additional cases not included in these latter reviews and reported since their publication.[4-7] These, added to the case presented herewith, bring the total of reported cases to 449.

According to the estimate of Devoe and Pratt,[8] heterotopic pregnancy might be expected to occur in one out of 30,000 pregnancies. If this estimate is correct, about 130 such cases should occur annually in the United States alone. Even if this estimate is high, it is evident that the actual number of cases far exceeds the reported cases and that the condition is not so very rare.

The outcome of the intrauterine pregnancy in the following case has prompted a limited search of the literature for similar cases with similar results without notable success. A rather high incidence of stillbirths and neonatal deaths in the case of the intrauterine twins is noted in some of the more recent reviews.[1, 3, 9] The extensive researches of Ingalls[10] and his associates have shown that most congenital anomalies originate as fetal manifestations of critical stress in pregnancy. They have produced specific anomalies in the central nervous systems and skeletons of mice by creating hypoxic stress at various stages of pregnancy. They concluded that a large class of congenital defects is preventable. They call for an attack on the problem in the human by the use on a combined front of the threefold forces of laboratory, clinical, and epidemiological methodologies. Although no positive conclusions can be drawn from the following case, it does provide clinical evidence which may, when combined with evidence from other cases, be useful in this program.

The patient, a 32-year-old white woman, had had two previous uncomplicated pregnancies with term deliveries of normal infants in 1948 and 1949. Her last normal menstrual period had begun Nov. 30, 1951. Following this, she had no bleeding and no other difficulties except mild cramping abdominal pain until the day of admission, Feb. 18, 1952. On this date, she noted the sudden onset of severe pain in the lower abdomen. This grew steadily worse and after 4 hours she was seen by her family physician who found her in shock and brought her immediately to our hospital.

Upon arrival the patient was in obviously severe distress. The skin was pale, cool, and moist. The pulse was rapid and thready, the blood pressure 70/50. The heart was normal

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except for tachycardia, the lungs were clear. No other significant physical findings were present except in the abdomen and pelvis where the extreme degree of tenderness and rigidity made examination without anesthesia useless. The hemoglobin was 8.4 Gm. per 100 c.c. The serologic test for syphilis was negative.

The patient was prepared immediately for operation and given intravenous fluids and blood with fairly rapid improvement in the blood pressure. Under general anesthesia, she was examined briefly and found to have a doughy mass filling the right side of the pelvis and cul-de-sac. The uterus was noted to be soft and symmetrically enlarged to a size commensurate with a pregnancy of 8 to 10 weeks' duration. Without further delay a laparotomy was done. At least 1,000 c.c. of fresh and clotted blood was found in the abdomen and pelvis. The right tube was found to have a ruptured fusiform enlargement 4 cm. in diameter in its ampullar portion. The enlargement of the uterus was confirmed on direct examination. Right salpingectomy was done. During and immediately following the operation a total of 2,000 c.c. of blood was given.

There was a slight amount of dark vaginal bleeding during the first two postoperative days. She was not given hormones. She had a febrile course during the first 3 days and was given penicillin. Otherwise her postoperative convalescence was uneventful. The urinary output was good. She was discharged on the ninth postoperative day.

The pathologist reported both a small fetus and placenta in the excised tube.

On March 31, 1952, she was found to have uterine enlargement consistent with a pregnancy of 16 weeks. She had had no bleeding nor other difficulties since leaving the hospital. She was followed through an apparently normal pregnancy until the thirtieth week. On July 7, 1952, she was found to have polyhydramnios as evidenced by the size of the abdomen and a 14 pound weight gain during the preceding 4 weeks. The blood pressure was normal; the urine negative. Fetal heart sounds were normal.

Two days later the patient went into labor and after 12 hours had a breech delivery of a female infant who weighed 1,710 grams. The diagnosis of hydrocephalus was made when the head failed to come into the pelvis. After drainage of a large amount of intracranial fluid it was delivered easily. The infant was dead.

The postpartum convalescence was uncomplicated.

Autopsy of the infant showed no anomalies other than the hydrocephalus and clubfeet.

I have followed this patient through two more pregnancies, entirely uncomplicated and resulting in spontaneous deliveries of normal infants at term.

Summary

A case of heterotopic pregnancy is reported in which the intrauterine fetus reached viability, but was hydrocephalic and died intra partum.

It is felt that this is a stage-specific acquired anomaly and may reasonably be attributed to anoxic stress in the mother at about the sixty-fifth day of pregnancy.

References

1. Zarou, C. S., and Sy, A.: Am. J. Obst. & Gynec. **64**: 1338, 1952.
2. Viviano, J. G.: Am. J. Obst. & Gynec. **72**: 191, 1956.
3. Vasicka, A. I., and Grable, E. E.: Obst. & Gynec. Surv. **11**: 603, 1956.
4. Lawson, J. G., and Chouler, F. J.: J. Obst. & Gynaec. Brit. Emp. **62**: 951, 1955.
5. Jacks, L. M.: M. J. Australia **42**: 1:536, 1955.
6. Selmeci, E., and Lakatos, G.: Orvosi hetil. (Budapest) **96**: 55, 1955.
7. de Moraes, A., and Ferrera, C.: An. brasil. ginec. **39**: 327, 1955.
8. Devoe, R. W., and Pratt, J. H.: Am. J. Obst. & Gynec. **56**: 1119, 1948.
9. Reeves, C. P., and Savarese, M. F. R.: Obst. & Gynec. **4**: 492, 1954.
10. Ingalls, T. H.: J. A. M. A. **161**: 1047, 1956.

MALIGNANT MESONEPHROMA OF THE LEFT BROAD LIGAMENT: A CASE REPORT*

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CYSTIC changes in the vestiges of the mesonephric and paramesonephric ducts of the broad ligament are frequently seen, but it is generally considered that malignant tumors of these structures are exceedingly rare. In 1948 Gardner, Greene, and Peckham[1] made an exhaustive study and report of the histogenesis of the various types of cysts which may be found in the broad ligament, including a description of the criteria for the differentiation of mesonephric and paramesonephric cysts. They reviewed a large number of cystic structures and changes in these ducts, but did not report any solid or malignant tumors.

In 1953 Lennox and Meagher[2] reported a case of paraovarian carcinoma, and stated that they had been unable to find any previous report of such a lesion. In their review of the literature, they were able to find only 2 cases of benign papillary paraovarian cysts, those of Nicholson in 1923 and Muller in 1942.

In 1954 Novak, Woodruff, and Novak[3] reviewed the literature and embryology of the female genitourinary system. They reported a small number of cases of rare pelvic tumors to establish their probable mesonephric origin and added 2 cases of benign solid tumors of the broad ligament.

A 37-year-old white woman (Case No. 22396), para ii, gravida iii, who had had one abortion, was first seen in our office on March 2, 1956, with the chief complaint of hemorrhage from the uterus.

The patient stated that on Feb. 25, 1956, she had begun what she thought was a normal menstrual period, although it was one week early. The flow was quite profuse with many clots, and she had rather severe pain in the lumbar region and in the lower portion of the abdomen.

A dilatation and curettage of the uterus had been performed in 1945 for spontaneous incomplete abortion, and a dilatation and curettage of the uterus with biopsy and conization of the cervix in 1952. The pathological report from this latter procedure showed hyperplasia of the endometrium and chronic cervicitis with acute purulent inflammation. In addition, the surgeon at this time stated that the uterus was of normal size and shape and there were no masses felt in the pelvis, adnexa, or cul-de-sac. The previous menstrual history was otherwise normal and there had been two full-term pregnancies, the most recent 9 years previously.

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At the time of examination, the uterus was noted to be anterior, enlarged approximately four times normal size, slightly nodular in the fundal portion. A mass was noted in the cul-de-sac, nodular, firm, slightly movable, about 4 to 6 cm. in diameter. Rectovaginal examination confirmed the pelvic findings.

Fig. 1.

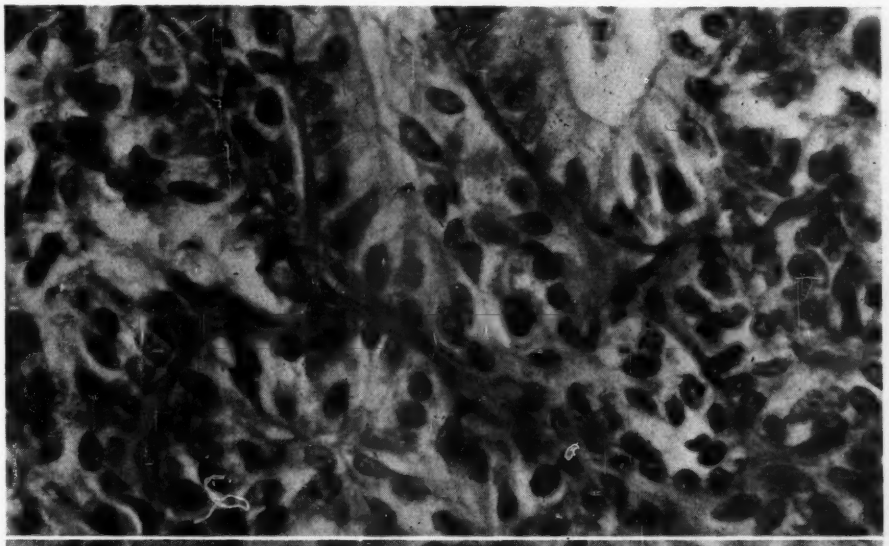

Fig. 2.

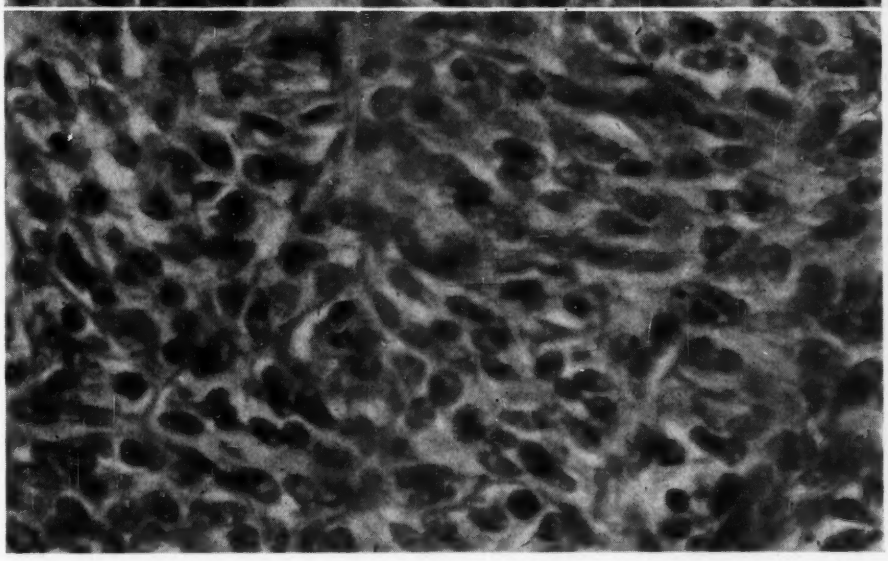

Fig. 1.—High-power photomicrograph showing cuboidal and columnar cells in definite tubular arrangement with vacuolization of the cytoplasm. (×40; reduced ¼.)

Fig. 2.—Low-power showing zigzag arrangement of more differentiated cells. (×10; reduced ¼.)

On admission to the hospital, laboratory findings showed a hemoglobin of 52 per cent and an erythrocyte count of 3.1 million. Other studies relative to general health were normal.

The patient received three transfusions of whole blood, after which the hemoglobin rose to 74 per cent. On March 5, 1956, dilatation and curettage of the uterus was performed,

with biopsy of the cervix. The report showed normal endometrium in the secretory phase and chronic cervicitis.

On March 7, an exploratory laparotomy was carried out. When the peritoneal cavity was opened, the uterus was seen to be approximately four times normal size, nodular in shape, and firm in consistency. The right and left tube and ovary were normal in appearance, size, and shape. Arising from the posterior leaf of the left broad ligament, from a 1½ cm. base, was a firm, nodular, encapsulated mass approximately 7 by 6 by 5 cm., which was adherent in the cul-de-sac by one small adhesion. The mass was dissected free from the cul-de-sac and brought into the operating field, when no evidence of any continuity with the left oviduct or left ovary could be demonstrated. The tumor was then removed. Because of the suspicious appearance of this lesion, the pathologist was consulted; a frozen section revealed probable adenocarcinoma. A total hysterectomy with bilateral salpingo-oophorectomy and appendectomy was performed. The peritoneum of the cul-de-sac was resected in the region of the attachment of the tumor to it.

The patient had a relatively uneventful postoperative course and was discharged home on the tenth postoperative day. At the most recent follow-up examination, on Jan. 22, 1957, she was in excellent health and there was no evidence of recurrence on either rectal or pelvic examination.

Pathology.—The initial pathology report by Dr. George Kerr showed malignant tumor of the left broad ligament, probably of mesonephric origin; multiple benign fibromyomas of the uterus; chronic cystic cervicitis; normal oviducts, ovaries, and appendix.

The external surface of the tumor was lobulated, with a thin, smooth, vascular capsule, yellowish tan in color, with a few hemorrhagic areas. On cut surface the tumor presented a fleshy light yellowish-pink appearance with eversion of its periphery showing it to be under moderate tension. The growth was for the most part solid but with a few small irregular areas of cystic degeneration.

Under the microscope there appeared to be two definite patterns: (1) a diffuse cellular tissue with spindle-shaped cells containing very prominent nuclei and relatively scant cytoplasm, with some attempt at formation of tubules; (2) better differentiated areas, with distinct tubules the individual cells of which appeared definitely epithelial in character. The mucicarmine stain failed to show the presence of mucicarminophilic material, but the fat stain showed many fat droplets in close association with the nuclei.

The pathological report by Dr. Saul Kay of the Medical College of Virginia was: "Mesonephroma (probably malignant) of the broad ligament."

The tumor slides and a portion of the tumor were also sent to the Ovarian Tumor Registry and a preliminary report by Dr. Emil Novak is as follows: "There would seem to be no question as to the malignancy of the lesion, which to me at least gives the impression of being a very solid type of adenocarcinoma, but I can imagine that there will be much uncertainty as to its histogenesis. Personally I would suspect the mesonephric vestiges which are frequently found in the broad ligament, but certainly I do not feel arbitrary on that point."

From these and other opinions we believe that this tumor is malignant, arising from the vestiges of the mesonephric system in the left broad ligament. Figs. 1 and 2 illustrate the microscopic appearance.

Summary

A neoplasm arising in the left broad ligament is reported as the sixth reported case of solid tumor, the second malignant one, of mesonephric origin arising in this area.

References

1. Gardner, G. H., Greene, R. R., and Peckham, B. M.: Am. J. Obst. & Gynec. 55: 917, 1948.
2. Lennox, B., and Meagher, D. J.: J. Obst. and Gynaec. Brit. Emp. 59: 783, 1953.
3. Novak, E., Woodruff, J. D., and Novak, E. R.: Am. J. Obst. & Gynec. 68: 1222, 1954.

Gynecology

EXPERIENCE IN A COMMUNITY HOSPITAL WITH MULTIVISCERAL PELVIC RESECTION FOR ADVANCED PELVIC CANCER

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PROGRESS reports dealing with the pelvic exenteration operation for advanced female genital cancer from university hospitals and special cancer centers urge that this procedure be restricted to institutions where availability of clinical material and adequate personnel permit critical evaluation. However, this attitude overlooks the fact that recurrent or residual carcinoma of the uterine cervix and associated adnexa presents a problem in many hospitals, particularly when previous adequate radiation therapy or limited surgery failed to achieve cure.

Since current radiation therapy yields a 5-year salvage rate of about 30 per cent in cervix cancer,[1] it is suggested that a new approach in this disease is warranted. Furthermore, unlike the inexorable local and/or metastatic progress of other common neoplasms, death in cancer of the cervix frequently occurs from progressive obstructive renal infection and terminal uremia while the disease is still localized in the pelvis.

Thus, while the need for a surgical technique to encompass multivisceral pelvic disease in selected cases of cervix cancer appears obvious, its adoption and acceptance will follow only when two questions are answered: Is it a safe operation? Can one expect significant palliation and chance for cure?

In order to answer these questions in a large, nonuniversity community hospital, multivisceral pelvic resection for advanced pelvic cancer was first started in 1948. Sufficient time has now elapsed to encourage us to feel that this procedure is safe, with reasonable mortality and morbidity rates, and palliation is significant, particularly in relieving local pelvic pain, eliminating

urinary and fecal fistulas, and decompressing obstructed ureters. Our series totals 44 multivisceral pelvic resections, of which 14 were total, and 30 were partial (see Table VI).

History

While Appleby[2] is generally credited with the first description of the multivisceral pelvic resection (for advanced rectal cancer in the male), Brunschwig[3] developed the first clinical investigative program for the management of advanced carcinoma of the cervix at the Memorial Cancer Center in New York. His recent report[4] detailing the results of 315 total and partial pelvic exenterations represents the largest experience in the surgical literature. Others[5-9] have reported smaller series and generally differ only in the management of transected ureters and technique of resection. The operative mortality rates from these institutions have been high, varying from 16 to 45 per cent, but significant palliation in terms of months has been achieved. While sufficient time has not elapsed to evaluate satisfactorily from all series the curability inherent in this operation, the available figures suggest a 15 per cent five-year survival.[4] It should be noted that this achievement in advanced pelvic disease exceeds that reported in advanced pulmonary, gastric, esophageal, and pancreatic neoplasms.

Material

Table I indicates that cancer of the cervix makes up 60 per cent of our series.

TABLE I. DISTRIBUTION OF CASES

Cancer of cervix	28
Cancer of corpus	3
Cancer of vagina	1
Cancer of ovary	7
Cancer of rectum	4
Cancer of bladder	1
Total	44

TABLE II. SYMPTOMS OF ADVANCED PELVIC CANCER

1. Bleeding	
Vaginal	15
Rectal	3
Vesical	2
2. Pain	
Sciatic	8
Pelvic (back)	23
Lower abdominal	20
3. Fistulas	
Rectal	5
Vesical	3
4. Obstruction	
Bladder base	11
Ureters	23
Rectum	7
5. Cachexia	9
6. Anemia	24

The majority of patients in this series were in the fourth and fifth decades of life, although 2 were in their thirties and 8 were above 60 years of age.

Only one patient was denied exploratory operation and she because of language barrier, socioeconomic factors, and age. Thirty-two others were subjected to exploratory laparotomy but deemed inoperable because of extrapelvic spread with hepatic, peritoneal, and serosal involvement. In this group, direct invasion of the iliopsoas muscle, lumbosacral plexus, and encasement of the external iliac artery were sufficient local reasons for denying the patient ablative surgery. No selection was used in this series beyond that of patient acceptance and absence of palpable disease outside of the pelvis. No patient rejected the operation. Furthermore, the diversity of pelvic neoplasms attests the lack of selection.

One cannot emphasize too strongly the necessity for complete understanding between patient, family, and surgeon concerning the magnitude of, and anatomical deficit created by, this operation. We believe the patient has the right to know the implications of this surgery, and have found the postoperative course smoother and follow-up assured once the patient's confidence is established.

It is apparent from Table II that the multiplicity of debilitating symptoms associated with advanced pelvic cancer will generally compel patients and families to accept operation. Narcotic addiction and semi-invalidism were commonly encountered.

Table III indicates the preoperative hazards in this series. Previous x-ray and radium therapy, obesity, and adhesions from former pelvic surgery all combine to prolong the operative time with the added menace of complications.

TABLE III. PREOPERATIVE HAZARDS

X-ray and/or radium	31
Adhesions from surgery	16
Obesity	16
Diabetes	3
Cirrhosis	1

Technique

Preoperative preparation is directed toward cardiovascular evaluation of the elderly patient, blood volume studies with appropriate replacement, intravenous pyelograms or cystoscopy and retrograde studies for evaluation of the bladder base and obstructed ureters, and, finally, adequate colon preparation. Preliminary electrolyte studies, chiefly of serum sodium, potassium, chloride, carbon dioxide combining power, and nonprotein nitrogen, serve as a useful base line for postoperative fluid and electrolyte replacement, particularly since we routinely use Miller-Abbott intubation in the immediate postoperative period.

The Anesthesia Service has been responsible for the careful preoperative assessment of these patients. Utilization of multiple agents to promote relaxation and minimize bleeding during this extensive procedure is of the greatest aid. Hypotension achieved with hexamethonium and allied drugs has made the deep pelvic operative field, in an obese patient previously treated by radiation and surgery, less vascular, thus permitting a more complete and safe operation.

At laparotomy, the neoplasm must be confined to the pelvis and must not involve the external iliac artery, iliopsoas muscle, and lumbosacral plexus to justify resection. Palpable liver metastases, and frozen section proof of metastatic para-aortic lymphadenopathy or serosal implants interdict surgery.

While we routinely utilized the one-stage, combined abdominoperineal approach early in this series, we currently favor the single-stage abdominal

supralevator procedure. It is our feeling that adding the perineal phase contributes to shock and greater morbidity, and protracts convalescence. Further, there appears to be no anatomical logic for adding perineal excision since cancer of the cervix, corpus uteri, and ovary does not commonly follow the lymphatics along the inferior hemorrhoidal vessels as is the case with advanced rectal adenocarcinoma. On the other hand, the lower midline approach permits one to clear the levator muscles of their areolar tissue and lymphatics, including removal of the middle hemorrhoidal vessels at or with the hypogastric vessels. When the internal iliac vessels (hypogastric) are involved by direct extension of disease or metastatic nodes, they are sacrificed and the lumbosacral plexus exposed and cleared.

Since we have eliminated the perineal phase, no patient has developed a perineal recurrence to this date. When rectal or pararectal extension of the neoplasm demands resection of lower sigmoid and upper rectum, we favor primary pelvic anastomosis of left colon to the short rectal stump at the levator level, in place of a permanent abdominal sigmoid colostomy. A complementary proximal decompressing cecostomy or transverse colostomy has not been added to this procedure.

We have also tested the several methods of handling the transected ureters. Table IV demonstrates our preference for the "ileal bladder." Originally, influenced by the technique of Brunschwig, we implanted the transected ureters into the permanent abdominal sigmoid colostomy, thus creating a sphincterless abdominal cloaca draining both feces and urine. We have abandoned this, since it was not only esthetically repugnant to the patients, but also was occasionally attended by ascending urinary tract infection. Nine patients in this series have had implantation of normal ureters into the intact or reconstructed sigmoid with normally functioning rectal sphincter. This procedure results in diarrhea, proctitis, hyperchloremic acidosis, and frequent bouts of ascending urinary tract infection with progressive renal damage of varying severity. Similar complications have been reported by Ferris and Odel.[10] In one patient, despite patent ureterosigmoid stomas, the severity of these symptoms made creation of an ileal bladder a lifesaving measure.

TABLE IV. METHODS OF URINARY DIVERSION

Abdominal cloaca, "wet colostomy"	4
Rectal cloaca, ureterosigmoidostomy	9
Ileal bladder, ureteroileostomy	21
Total	34

Our current preference is to make an ileal bladder, utilizing the technique described by Bricker[11] of implanting all ureters, whether normal, dilated, or nonfunctioning (as demonstrated by intravenous pyelograms), into a loop of defunctionalized ileum. Of 21 patients in whom we have created the ileal bladder, 2 required preliminary nephrostomy to relieve uremia and control urinary tract infection before radical pelvic surgery could be carried out.

TABLE V. RESTORATION OF RENAL FUNCTION

	NONFUNCTIONING KIDNEY	HYDRONEPHROSIS
Preoperatively	17	9
Postoperatively	1 (tuberculosis)	5

Table V demonstrates the improvement of renal function as demonstrated by intravenous pyelograms following resection of the ureter-obstructing pelvic cancer, and implantation of the ureters into the sigmoid or defunctionalized

ileal loop. No patient in the ileal bladder series has developed hyperchloremic acidosis and only 4 patients developed clinical evidence of ascending urinary tract infection. Urine cultures from the hydronephrotic and poorly functioning renal units at the time of transplantation were sterile in all instances but one. Our experience with the ileal bladder technique is the subject of a separate report.[12]

Table VI records the number and character of exenterations performed in this institution. The ratio of 2:1 between partial and total multivisceral resections is noted. In all instances bilateral iliac, obturator, paracervical, and paravaginal lymphatics were removed. If, however, an anterior lesion involved bladder and/or ureters without rectal involvement, the latter was spared. On the other hand, if a posterior lesion required sacrifice of rectum and sigmoid, but did not involve the bladder and ureters, cystectomy was not performed.

TABLE VI. TYPE OF OPERATION

Total pelvic exenteration		14
Bladder		
Rectum		
Radical hysterectomy		
Bilateral iliac-obturator lymph gland resection		
Bilateral ureterosigmoidostomy or ileostomy		
Partial pelvic exenteration		
Anterior	21	30
Posterior	9	
Bladder or rectum and small intestine		
Radical hysterectomy		
Bilateral iliac-obturator lymphadenectomy		
Bilateral ureterosigmoidostomy or ileostomy		
Total		44

Postoperative Care

We have learned several lessons in the postoperative care of this group of patients. No effort should be made to conserve pelvic peritoneum, nor should one attempt to reperitonize the pelvis. If an adequate resection has been carried out, the pelvic cavity will be completely free of peritoneum from the bifurcation of common iliac vessels to levator muscles. Adequate drainage of this large raw pelvis is established through the open vaginal cuff. We have demonstrated that this unperitonized cavity and the denuded ureters will be reperitonized several months later as demonstrated by subsequent exploratory operations for recurrent disease or intestinal obstruction.

Prophylactic Miller-Abbott intubation started on the first postoperative day decompresses the ileoileostomy suture line (resulting from creation of the ileal bladder) and minimizes the tendency toward obstruction of the small intestine from adhesive bands and peritoneal exudate. Early in this series, before routine postoperative decompression, 2 patients developed obstruction of the small intestine in the immediate postoperative period. This complication has occurred but once since intubation has been instituted.

The serum electrolytes are checked every 2 days after operation, and deficits and excesses appropriately corrected until normal peristalsis is present and oral alimentation is instituted (generally 5 to 7 days). Catheter drainage of the ileal bladder abdominal stoma serves to keep the patient dry and records urine output. Follow-up intravenous pyelograms are obtained before discharge from hospital. A watertight urinary receptacle (utilizing a rubber bag with adhesive skin cement) is fitted to the permanent ileal stoma in the right lower quadrant after skin sutures are removed (7 to 10 days).

Complications

Complications incident to this series are listed in Table VII. Despite postoperative immobilization and considerable trauma to iliac veins inherent in pelvic dissection, only one instance of clinically demonstrable phlebothrombosis and pulmonary embolus was noted which was fatal. Edema of the legs was constant in instances where the external vein was sacrificed (3 patients). Appropriate antibiotics, based on baceriological cultures and sensitivity studies of pelvic and peritoneal exudates, routine postoperative intubation of the small intestine with close control of electrolyte and fluid balance, and improvement of ureteroileal anastomosis techniques should minimize the avoidable complications.

TABLE VII. POSTOPERATIVE COMPLICATIONS

Obstruction of large intestine	1
Obstruction of small intestine	4
Perineal ureteral fistula	2*
Perineal fecal fistula	4
Suppurative pyelonephritis	1
Hemorrhage	2*
Hemolytic staphylococcus enteritis	1

*One death from each complication.

Mortality

Four patients in this group of 44 failed to survive the operation, resulting in a mortality rate of 9 per cent.

The first death in this series occurred on the fifth postoperative day in our third patient, caused by dehiscence of a ureterosigmoid anastomosis with subsequent peritonitis as confirmed by post mortem. Subsequently, 29 consecutive pelvic exenterations were done without a death. The second death occurred in the recovery room 4 hours after operation in a patient who had suffered a near-fatal hemorrhage 4 days previously from a radiation-resistant cancer of the cervix. At post mortem, no opening of a major vessel was found responsible for a 500 c.c. blood clot in the pelvis. Two other deaths are detailed in Table VIII. The mortality rates of 16 to 45 per cent for this operation reported from medical centers in both England and the United States have been largely attributable to shock, hemorrhage, uremia, peritonitis, and pyelonephritis. We believe that these may have been decreased with increasing experience.

TABLE VIII. OPERATIVE MORTALITY, 1 TO 23 DAYS POST OPERATION

SERIES NO. OF PATIENT	AGE	OPERATION	FINDINGS AT AUTOPSY
No. 3	45	Total pelvic exenteration	Tension at ureterocolon anastomosis with dehiscence and urinary peritonitis, fifth postoperative day
No. 34	50	Total pelvic exenteration	Patient suddenly died 4 hours after operation in recovery room with no apparent cause for death on careful search at autopsy
No. 39	67	Anterior pelvic exenteration	Developed pulmonary emboli on fifth postoperative day and died on eighth day with autopsy findings of bilateral massive pulmonary emboli
No. 42	47	Anterior pelvic exenteration	Only patient in series to receive intraperitoneal nitrogen mustard into raw pelvis (30 mg.). Autopsy findings revealed marked malacia of ileal loop lying in pelvis with peritonitis, hemorrhage, and resulting fecal fistula, twenty-third postoperative day

Of the 28 patients who are dead, local recurrence or metastatic disease was noted clinically or post mortem in all but one. The majority died within one year, and in this group palliation could be measured only in months. The fatal progress of extrapelvic metastatic disease in this series points to our inadequacy in accurately evaluating abdominal findings at laparotomy. On the other hand, preoperative vaginal-abdominal evaluation of the "frozen pelvis" can be misleading. In several such instances, laparotomy has revealed not only that the disease was confined to the pelvis but was completely resectable. It should be emphasized that all patients with advanced cancer of the cervix associated with metastatic local lymphadenopathy have died, which is in accordance with the experience of other clinics.

We have been encouraged, however, by the 16 survivors at this date. All are clinically free of disease. Not one is an invalid or bedridden, and the majority are actively engaged in their daily tasks. Restoration to useful life for periods of months to years in this group encourages us to believe that this effort is worthy of continued trial. We believe that 7 patients (15 per cent) surviving over 3 years with 3 (7 per cent) passing the 5 year follow-up period justify continued interest in this type of surgery. Two of the 3 survivors for 5 years and the single 4 year survivor had total pelvic exenteration. The remaining 13 patients have had partial exenteration, sparing rectum or bladder.

End Results

The end results of this effort are shown in Table IX.

TABLE IX. END RESULTS (5 YEAR SURVIVAL = 7%)

	YEARS						
	0-1	1-2	2-3	3-4	4-5	5	TOTAL
Living	6	1	2	3	1	3	16
Dead							28

Comment

It is our hope that this series demonstrates that multivisceral pelvic resection can be offered the female patient with advanced pelvic cancer either as the primary treatment or after radiation failure, in the expectation that good palliation may be possible with reasonable morbidity and mortality rates. Future follow-up will determine how many patients will be cured. A 5 year survival rate of 16 per cent has been reported by Brunschwig[4] from the series referred to above. Since carcinoma of uterine cervix tends to remain localized in the pelvis, it appears to be a most favorable pelvic lesion for resection, particularly if adjacent nodes are not involved. Neoplasms of the ovary, corpus uteri, bladder, and rectosigmoid are prone to peritoneal, hepatic, pulmonary, perineural, and extrapelvic lymph node spread when the primary lesion achieves such dimensions as to require radical pelvic surgery. Despite this, careful selection based on the variability of behavior of neoplastic disease may yield some advanced neoplasms of the ovary and corpus uteri for surgery with resulting prolonged palliation and even cure. Specifically, when the interval between initial therapy (radiation and/or surgery) and recurrence is several years in a patient in good physical condition willing to accept

radical surgery and without demonstrable evidence of extrapelvic spread from the primary pelvic neoplasm, one is certainly justified in recommending this procedure.

Constant pelvic and low back pain, urinary and/or fecal fistulas, obstructive uropathy, vaginal bleeding, malodorous discharge, narcotic addiction, and debility are corrected totally or partially by this surgical procedure. It has also been gratifying to note the remarkable return of function (Table V) in poor-to-nonfunctioning renal units after relief of obstruction by multivisceral pelvic resection and appropriate ureteral transplantation.

Probably the ideal candidates for this operation, to whom comfortable and useful life can be assured, is to be found in that small group of women where radiation therapy for cervix cancer has achieved cure, but concomitantly produced rectal and/or urinary fistulas due to radiation necrosis; or fibrosis stricture of ureters with progressive uropathy and small or large bowel obstruction. Two patients in our group presented such a problem and have been restored to health. One other exenteration series[13] reports 10 such cases.

A report from Stockholm[14] suggests that radiation resistance of cervix cancer and incurability may be synonymous. Heyman postulates that those cervix neoplasms which fail to regress with adequate radiation therapy might be inherently more malignant and accordingly incurable with any modality of therapy, including surgery. This has not been borne out in larger series, particularly in the absence of regional nodal metastases.

We were also surprised to note that but 8 of our 24 advanced cases of cervix neoplasm demonstrated metastases to adjacent lymph nodes. This modest figure (33 per cent) is at variance with that expected for advanced cervix cancer (League of Nations Stages III-IV) where 50 to 70 per cent regional node metastases have been recorded. While our figure may be statistically invalid because of the small number of cases, one cannot ignore the recent report of the Grahams,[15] who suggest that preoperative pelvic irradiation may have a cancerocidal effect on some pelvic lymph node metastases. All but 2 of our patients with cervix cancer had preoperative external x-ray therapy supplemented by interstitial radium.

Last, it is our impression that more general adoption of the multivisceral pelvic resection will be retarded by the inflexibility of surgical subspecialties. A single operator should properly assume responsibility for the conduct of the operation. However, the multiplicity of structures involved, i.e., bladder, ureters, uterus and associated adnexa, adjacent lymphatics, as well as small and large intestines, place the specialties of urology, gynecology, and surgery in competition with one another during a single operation. Traditionally, each surgical specialist has been reluctant to encroach upon the anatomical field of his colleague. Accordingly, this operation is often regarded as too formidable for any one surgeon, or suffers because of division of responsibility at or after operation. More adequate surgical training in the surgical subspecialties of urology and gynecology, with added experience utilizing the

experimental surgical laboratory or even postmortem material, might overcome this impasse. These deficiencies in surgical training have recently been discussed by Burch.[16]

We believe this small series demonstrates the practicality of conducting so-called "superradical" pelvic surgery safely in a community, nonuniversity hospital. We are hopeful that with continued experience in preoperative evaluation and selection, as well as technical performance, mortality and morbidity will remain low. Furthermore, there is the probability that as experience with the surgical resection improves, a higher salvage rate with lower local recurrence should be anticipated. There is little doubt in our minds that we have continually improved upon details of dissection, particularly in the area of the obturator space and lumbosacral nerve plexus, and in the performance of ureteroileal anastomosis.

Summary

1. A series of multivisceral pelvic resections for advanced pelvic cancer is presented from a community, nonuniversity hospital.

2. A mortality rate of 9 per cent is recorded with a concomitantly low morbidity-complication rate.

3. The evolution of this surgical technique with appropriate safeguards is described.

4. Criteria of operability with anticipated palliation and potential cure are discussed.

References

1. Morris, J. McL., and Meigs, J. V.: Surg., Gynec. & Obst. **90**: 135, 1950.
2. Appleby, L. H.: Am. J. Surg. **79**: 57, 1950.
3. Brunschwig, A., and Pierce, V. K.: Cancer **3**: 972, 1950.
4. Brunschwig, A., and Daniel, W.: Surg., Gynec. & Obst. **99**: 324, 1954.
5. Ulfelder, H., and Meigs, J. V.: New England J. Med. **246**: 243, 1952.
6. Brintnall, E. S., and Flocks, R. H.: Arch. Surg. **61**: 851, 1950.
7. Parsons, L. G., and Bell, J. W.: Cancer **3**: 205, 1950.
8. Bricker, E. M., and Modlin, John: Surgery **30**: 76, 1951.
9. Blaikley, J. B.: Proc. Roy. Soc. Med. **46**: 753, 1953.
10. Ferris, D. O., and Odel, H. M.: J. A. M. A. **142**: 634, 1950.
11. Bricker, E. M.: S. Clin. North America **30**: 1511, 1950.
12. Wawro, N. W.: Ann. Surg. **144**: 829, 1956.
13. Brunschwig, A.: Surg., Gynec. & Obst. **93**: 431, 1951.
14. Heyman, J., and Belonoschkin, B.: Acta chir. scandinav. **98**: 489, 1949.
15. Graham, J. B., and Graham, R. M.: Surg., Gynec. & Obst. **100**: 149, 1955.
16. Burch, J. C.: Ann. Surg. **141**: 573, 1955.

SOME OBSERVATIONS ON MODERN TRENDS IN THE DIAGNOSIS AND MANAGEMENT OF GYNECOLOGICAL CANCER*

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IT IS not my purpose tonight, nor is it within my ability, to sift the newer ideas on cancer of the female genitals and pool individual concepts so as to produce a compact treatment package for 1957. I merely will endeavor as Director of one of the Ontario Cancer Foundation's eight clinics to portray our own Clinic's reaction to certain modern trends in both diagnosis and therapy, and this I do in modesty, being fully cognizant of the original and superb leadership many members of this Society have given through the years.

I am not clear whether it was Cleaves or Abbé, both of New York, who first inserted radium into the cervix with malignancy, but the initiative of Dr. Howard A. Kelly certainly revealed that radium was an effective alternative to the Wertheim operation. It was he who in later years urged irradiation for the fibroid uterus. During my residency with him in 1930, I sensed a feeling of conservatism for well do I recall his saying, "Doctor, perhaps I did more than anyone else in the country to advance the operation of uterine suspension, and probably it was the worst thing I ever did." It was during that year that a goodly number of Tom Cullen's patients with recurrences after the Wertheim operation were referred for radium. Is it not very natural that I, too, from that memorable association, leaned toward irradiation and conservatism? In fact, those years implanted into my professional system a seed which ultimately germinated into a basic principle that dominates the thinking of our London Cancer Clinic today, "Do a minimum that is compatible with diagnosis and cure"; and yet, with expanding radiotherapy and extended surgery the ever-tantalizing decision which confronts us is, just what is that minimum?

For purposes of discussion permit me to cite and weave into the context of this thesis five major developments since 1930, which have appreciably altered our attitude and actions toward gynecological cancer: *exfoliative cytology,* a *system of radium dosage, supervoltage, supersurgery,* and the *isotopes.*

Carcinoma of the Cervix

Exfoliative Cytology.—From a precarious start some fifteen years ago, exfoliative cytology is now securely entrenched as a diagnostic procedure. It has its false positives, as occasionally in pregnancy and chronic cervicitis, and

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its false negatives, particularly in carcinoma of the fundus, but an awareness of these and a knowledge of the dexterity of one's pathologist combine to make the cell reveal what already has taken or will take place neoplastically. It is the extended arm of pathology without which we would feel lost. Having had no wide personal experience with the cervical scrape for histological processing, we are unable to compare its value with that of the smear. When the cervix appears normal the smear is obtained by, and made from, the Ayre spatula. Should there be any erosion or questionable patchy mucosal thickening, one or more punch biopsies are taken as well. The "vaginal pool" is used less and less, chiefly because of the high percentage of inaccuracy in our hands in the cytological diagnosis of carcinoma of the fundus. Professor J. H. Fisher's smear volume is just beyond the 5,000 but his contribution to our Clinic through cytology in so many sites is immeasurable.

Although we as a clinic group rely on smear supplemented by biopsy when indicated, a quick glance at the Foundation's free biopsy service for 1955 reveals a different trend of action throughout the Province.

TABLE I. THE ONTARIO CANCER FOUNDATION FREE BIOPSY SERVICE

1955 TOTAL	MALIGNANT	POSITIVE
18,018	3,179	17.6%

Cervical Studies

	BIOPSIES		AYRE SCRAPES		TOTAL	
YEAR	NO.	POSITIVE	NO.	POSITIVE	NO.	POSITIVE
1954	2,460	3.98%	3,096	1.56%	6,366	2.50%
1955	2,422	2.89%	4,057	0.74%	6,479	1.54%

Some 18,018 biopsies were taken by physicians, dentists, and clinics. Cytology not being paid for, it is interesting to note that of 6,479 total cervical examinations, 4,057 were scrapes, of which 0.74 per cent were positive. This is comparable to the results of other broad screening surveys.

Cullen surely started something in 1913 when he broke with traditional medical etiquette by endorsing that first popular article on cancer which appeared in *The Ladies Home Journal.* It was not done impulsively, but after due deliberation and correspondence when he was Chairman of the Cancer Campaign Committee of the Congress of Surgeons of North America. He started the pendulum of early diagnosis moving, and forty-four years later it flits to and fro in crescendo rhythm and momentum.

It is naturally obvious that with the expanding use of Papanicolaou smears, scrapes, and biopsies, associated with the tremendous increase in regular pelvic examinations, silent cancer is being uncovered, the most intriguing of which is carcinoma in situ.

This to us is a pathological entity, and is dealt with positively. Let us, in the first instance, be sure that it is truly in situ. You have all seen the surgically removed specimen which had extended well beyond the preinvasive boundaries. Having proved its intraepidermal position, we recognize three groups, with management as follows:

1. The young woman anxious for a family, or a bigger family, for whom conization is acceptable.

2. The young woman whose family interests are satisfied, for whom hysterectomy is acceptable.

3. The older patient on whom radium is used with dosage slightly curtailed, thereby practically assuring no untoward complications.

Our gynecological colleagues are quite willing to agree in principle to such a scheme, yet verge from it as human nature and circumstances so dictate. Adhering to our Clinic dictum, "Do a minimum that is compatible with cure," I confess with few exceptions, in my own hands, conization is the order of the day.

A System of Radium Dosage.—Having due regard for the stalwarts in radiotherapy and physics both on this continent and abroad, whose contributions lead us away from empiricism, I will quote my mentors only, Paterson and Parker,[1] and Tod and Meredith[2] of Manchester. The gamma roentgen replaced the milligram hour; for cancer of the uterine cervix, the paracervical triangle was conceived, while points A and B took on significance from the standpoint of desired dosage. Point A as initially described represented the crossing of ureter and uterine artery, positioned 2 cm. from the midline and 2 cm. above the lateral fornix, point B corresponding to the side wall of the pelvis 5 cm. from the midline, and on the same level as point A.

Table A is a study of dosage delivered to points A and B by radium alone, radium plus x-ray, and radium plus cobalt.[60] A modified Regaud radium technique is used and to achieve the gamma roentgen dosage indicated at the cardinal points the average patient receives 4,000 mg. hr. intrauterine and 4,000 mg. hr. vaginally in two applications over a 10 to 12 day period. It is immediately apparent that by the monochromatic beam from cobalt[60] a substantial dosage increase is possible to the parametria and in 15 treatment days as opposed to 17 to 20 by 250 kv. x-ray.

TABLE A. RADIUM DOSAGE IN CANCER OF THE CERVIX

METHOD OF TREATMENT	POINT A	POINT B
Radium alone (Regaud)	5,500 r	1,800 r
Radium plus x-ray	8,120 r	4,300 r
Radium plus cobalt[60]	8,970 r	5,800 r

TABLE II. FIVE-YEAR RESULT OF TREATMENT AS SUBMITTED TO TENTH VOLUME (HEYMAN)

STAGE	NO. PATIENTS TREATED			RELATIVE APPARENT RECOVERY RATE AT THE END OF		
	1944-1948	1942-1946	1939-1943	5 YEARS (%)	7 YEARS (%)	10 YEARS (%)
I	30	22	15	73.3	86.4	100.0
II	65	70	49	49.2	44.3	40.8
III	26	16	14	34.6	25.0	--
IV	11	9	7	0.	0.	0.
I-IV	132	117	85	47.7	46.2	44.7

TABLE III. FIVE-YEAR RESULT OF TREATMENT AS SUBMITTED TO SEVENTH VOLUME (HEYMAN)

STAGE	NO. PATIENTS TREATED			RELATIVE APPARENT RECOVERY RATE AT THE END OF		
	1941-1945	1939-1943	1936-1940	5 YEARS (%)	7 YEARS (%)	10 YEARS (%)
I	16	15	-	93.8	100.0	-
II	64	49	-	51.6	42.9	-
III	15	14	-	20.0	-	-
IV	5	7	-	0.0	0.0	-
I-IV	100	85	-	51.0	45.9	-

Table II shows our figures on the cervix as recorded in the *Tenth Annual Report* as compiled by Heyman.[3] These compare very favorably with figures

from the top few treatment centers but we have slipped a little from the *Seventh Report* recorded in Tables III and IV.

These results with cancer of the cervix, although leaving much to be desired, have entrenched irradiation therapy as the prime mode of attack in the London Centre, which indeed applies to the eight clinics of the Province.

TABLE IV. TABLE FROM SEVENTH ANNUAL REPORT (HEYMAN) ON RESULTS OF RADIOTHERAPY IN CARCINOMA OF THE UTERINE CERVIX. FIVE-YEAR RESULT OF TREATMENT

	65 CENTERS REPORTING		LONDON ONTARIO CANADA	
STAGE	NO. PATIENTS TREATED	RELATIVE APPARENT RECOVERY RATE (%)	NO. PATIENTS TREATED	RELATIVE APPARENT RECOVERY RATE (%)
I	10,582	58.7	16	93.8
II	23,190	40.0	64	51.6
III	22,911	21.8	15	20.0
IV	7,529	6.3	5	0.0
Unclassified	24			
Total	64,236	32.6	100	51.0

Supervoltage.—At the present time our basic treatment is by radium and cobalt.[60] Teletherapy truly is a most satisfying form of external irradiation from the clinical standpoint. The depth dose is higher, the skin reactions are faint, systemic upsets are minimal, and associated enteritis is most noticeably lessened as compared with that caused by conventional x-ray. Although we were privileged to be the first to use cobalt[60] teletherapy clinically, on Oct. 27, 1951,[4] it is only since early 1956 that this form of supervoltage has been used routinely for our patients with cancer of the cervix and I am unable to speak either of results or of late complications. One can, however, surmise that complications will be less and if increased parametrial dosage is of any biological value the trend to a better survival rate, even if slight, should appear. Our hopes for an improved survival rate rest in a better application of modern radium dosage, the substitution of cobalt[60] for x-ray, and attention to selectivity in surgical procedures.

From an observation on oral carcinoma[5] we find ourselves encouraged over the increased possibility of sterilizing the solitary lymph node containing malignancy. Of 50 oral cases which we treated radically by cobalt[60] beam therapy, 9 had a clinically positive solitary node sufficiently close to the primary disease to be included in the treated volume. One patient died of cancer, one died of intercurrent disease without cancer at autopsy, while 7 have been without disease for 18 to 45 months. None were operated upon. Cancer of the oral mucosa being histogenetically akin to epidermoid carcinoma of the cervix, you will readily appreciate our basis for optimism in substituting cobalt[60] for x-ray, particularly in the Stage I and II disease.

Be this as it may, our experience with cobalt[60] in the recurrent case with parametrial solidity has not been encouraging. It is true a dosage to midparametrium can be achieved through treacherous skin not possible by conventional x-ray. Studying a small group has forced us to realize that although palliation is possible and occasionally dramatic, as a rule it is not lasting. This, although disappointing, was not surprising and, as in the past when chagrined by failure, we continue to scan the horizon for chemical or physical agents which will favorably alter the sensitivity of tumors differentially as compared with their adjacent stroma. Meanwhile, we are reimpressed with the importance of a rigid follow-up regime, and a sane reappraisal of the place of radical surgery, either alone or in combination with irradiation, as the initial treatment, or for recurrence.

Supersurgery.—Our Clinic's experience with supersurgical procedures is far too limited to justify comment; suffice it to say we are keenly aware of the distress associated with advancing disease, and of the bold surgical approaches initiated by Brunschwig[6] to combat such misery, and we do not back away from any surgical obligations in individual instances. Lessons learned from irradiation procedures, however, have altered our basic radiotherapeutic thinking as of this date, as follows:

1. In the cervix with Stage II disease with invasion well up the endometrium irradiation is planned first, followed by the Wertheim operation.
2. The cervix with Stage II disease, with narrow vagina, contracted invaded vault, where radium distribution in relation to tumor is bound to be irregular, and dosage in relation to point A bound to be low, is a candidate for the Wertheim operation.
3. The Stage III case with a solitary node on the pelvic wall is also given complete irradiation first, followed by operation.
4. The cervix with Stage I or II disease with a questionable or definite adnexal mass is irradiated and operated upon.
5. Hysterocystectomy may well prove to be the better management for the patient with parametrial mobility, yet with true bladder invasion.
6. The recurrence or necrosis in the vault deserves investigation, biopsy, desiccation, perhaps conization, and, depending on the findings, meticulous surveillance with appropriate surgery in mind.

Such is our positive thinking with our minds wide open, yet not too impressed with the value of major palliative procedures for advanced or recurrent disease, unless for bladder or rectal involvement.

Carcinoma of the Corpus

Whereas irradiation forms the bulwark of therapy in carcinoma of the cervix, the principle of preoperative radium for carcinoma of the corpus uteri has been well established in our Provincial Centres for some twenty years. It is my understanding that Arneson[7] and Scheffey[8] of this country, being impressed by Heyman's use of radium alone, initiated the principle of the "planned" radium-surgery technique. There is radiobiological evidence in support of the theories behind the use of preoperative irradiation, and indeed I believe favorable clinical evidence is gradually accumulating, although it is difficult to assemble in quantities data of statistical value for different sites. The primary biological effect is the lethal influence of ionizing rays on the tumor cell and, when applied clinically to corpus carcinoma, authors agree that a high proportion of the specimens become free of cancer. This naturally varies with the stage of the disease; no residual tumor was found in at least 30 per cent of Cosbie's[9] series, while Schmitz[10] reported 76 per cent destruction of tumor in a series of 35 cases. The secondary indirect effects apply first to irradiated stroma which experimentally shows resistance to the implanted tumor cell, and, second, to the devitalized cell which if embolized may fail either to take or reproduce.

The following tables are based on pooled data (unpublished) from seven Ontario Cancer Clinics, covering the period 1937 to 1948, presented at a Symposium on Carcinoma of the Fundus Uteri held in Windsor, Ontario, in 1954, under the auspices of the Ontario Cancer Treatment and Research Foundation.[14]

Table V is an analysis of survival in 636 primary cases, all stages, treated between the years 1937 and 1948. "Primary" case implies that the patient registered at the Clinics has had no previous treatment. A "previous" case implies that the patient when registered at the Clinics was clinically free of disease, having had initial treatment elsewhere.

TABLE V. SURVIVAL IN 636 PRIMARY CASES OF CARCINOMA OF THE FUNDUS AFTER BEGINNING OF TREATMENT

METHOD OF TREATMENT	NO. CASES REVIEWED	CRUDE 5 YEAR SURVIVAL RATE (%)
X-ray alone	93	20.4
Radium alone	171	40.9
X-ray and radium	166	31.9
Surgery alone	20	70.0
Preoperative radiation, panhysterectomy	103	77.7
Preoperative radiation, subtotal hysterectomy, or not stated	40	75.0
Panhysterectomy, postoperative radiation	9	22.2
Subtotal hysterectomy (or not stated), postoperative radiation	9	44.4
Pre- and postoperative radiation, panhysterectomy	6	66.7
Pre- and postoperative radiation, subtotal hysterectomy, or not stated	8	50.0
Other methods	3	33.3
Not treated	8	0.0
Total primary cases	636	44.2

Table VI records the results by radium alone. The 61.3 per cent corrected survival rate surely indicates a tumor sterilization in an estimated 50 per cent, allowing for a limited recurrence group beyond the 5 year period.

TABLE VI. FIVE-YEAR SURVIVAL IN 172 CASES OF CARCINOMA OF THE FUNDUS TREATED BY RADIUM ALONE

STAGE	NO. REVIEWED	CRUDE SURVIVAL RATE (%)	CORRECTED SURVIVAL RATE (%)
I	57	52.6	61.3
II	20	45.0	53.8
III	5	-	-
IV	2	-	-
Not stated	88	36.4	43.3
Total	172*	41.3	49.1

*171 primary cases, 1 previous case.

Table VII, with only 20 strictly surgical cases, is a small group to evaluate favorably or otherwise, but the trend of 77.6 per cent crude survival is in the right direction.

TABLE VII. FIVE-YEAR SURVIVAL IN 20 PRIMARY CASES OF CARCINOMA OF THE FUNDUS TREATED BY OPERATION ALONE

STAGE	NO. REVIEWED	NO. KNOWN ALIVE	CRUDE SURVIVAL RATE (%)	CORRECTED SURVIVAL RATE (%)
I	9	5	-	-
II	4	4	-	-
III	-	-	-	-
IV	-	-	-	-
Not stated	7	5	-	-
Total	20	14	70.0	77.6

Table VIII is a highly encouraging analysis of "planned" treatment of preoperative radiation and panhysterectomy. A Wertheim operation was seldom done.

TABLE VIII. FIVE-YEAR SURVIVAL IN 103 PRIMARY CASES OF CARCINOMA OF THE FUNDUS TREATED BY PREOPERATIVE RADIATION AND PANHYSTERECTOMY

STAGE	NO. REVIEWED	CRUDE SURVIVAL RATE (%)	CORRECTED SURVIVAL (RATE %)
I	41	80.5	87.6
II	13	69.2	74.8
III	2	-	-
IV	-	-	-
Not stated	47	78.7	86.3
Total	103	77.7	84.9

Table IX portays a survial picture by panhysterectomy and postoperative irradiation.

TABLE IX. FIVE-YEAR SURVIVAL IN 118 CASES OF CARCINOMA OF THE FUNDUS TREATED BY POSTOPERATIVE RADIATION AND PANHYSTERECTOMY

STAGE	NO. REVIEWED	CRUDE SURVIVAL RATE (%)	CORRECTED SURVIVAL (RATE %)
I	26	57.7	62.2
II	18	61.1	66.1
III	4	-	-
IV	1	-	-
Not stated	69	62.3	67.1
Total	118*	61.9	66.7

*9 primary cases, 109 previous cases.

The Ontario experience favors the combined radium-surgery approach for operable carcinoma of the endometrium. The radium technique varies by Centre, and radium in the vaginal vault has not been routine. Intrauterine radium is arranged by multiple or tandem sources to deliver approximately 6,000 r, 2 cm. from the applicator, which is 3,600 to 4,000 in terms of mg. hr. Operation follows in 6 to 8 weeks. Should the lesion be questionably operable a full series of cobalt^{60} radiation is delivered to the pelvis following radium, and the patient is reviewed for hysterectomy in 8 to 12 weeks.

One is hardly justified in stating that irradiation plays a curative role in the extremely early case, with low-grade scant curettings and a small firm uterus, but the combined procedure is so well established that seldom is it veered from in the Ontario Centres. We await with interest the figures to come from a Wertheim type of procedure on this group.

Carcinoma of the Ovary

Our plan of action for early ovarian cancer is in a stage of negotiation for it is seldom as a Clinic group that we are brought into conference, prior to laparotomy. Hoping for benignancy regardless of the size of the tumor, the patient is operated upon, and with both gross and microscopic data available we are called upon for assistance. Probably this is characteristic the country over and pretty old fashioned. Under such a regime between 1937 and 1951, 83 patients with recurrences, residual, and postoperative cases were referred for x-ray therapy. Twenty-two patients, or 26 per cent, are alive and well,

5 to 19 years (Table X). I suspect that this percentage approximates the average but until such a time as there is more uniform agreement on staging and microscopic classification, comparative figures on results in therapy of ovarian cancer will continue as an amusing statistical puzzle.

TABLE X. CARCINOMA OF THE OVARY AT THE LONDON CLINIC

METHOD OF TREATMENT	NO. CASES	NO. DEAD	SURVIVAL
X-Ray Therapy, 1937-1951.—			
Postoperative, advanced, and recurrent	83	61	22 (26%) 5-19 years
Cobalt^{60} Beam Therapy, 1951-1953.—			
Postoperative	26	12	14 (53.8%) 3-5 years
Advanced and recurrent	26	22	4 (15.4%) 3-5 years
Total	52	34	18 (34.6%) 3-5 years

Fig. 1 illustrates the physical advantage of cobalt^{60} over x-ray therapy in terms of depth or central tumor dosage. Furthermore, a pelvic tumor dose of 3,500 r is achieved in 3 weeks as compared with 2,760 r in 4 weeks by x-ray. As in cancer of the cervix, one can postulate a fractional increase in survival if added dosage in the cobalt^{60} quality range is of positive significance; however, well-differentiated carcinoma of ovary is seriously radioresistant and any increased survival may well be related to the less common, sensitive, anaplastic types and the granulosa-cell group, perhaps even the radioresistant forms where the host resistance is inordinately high.

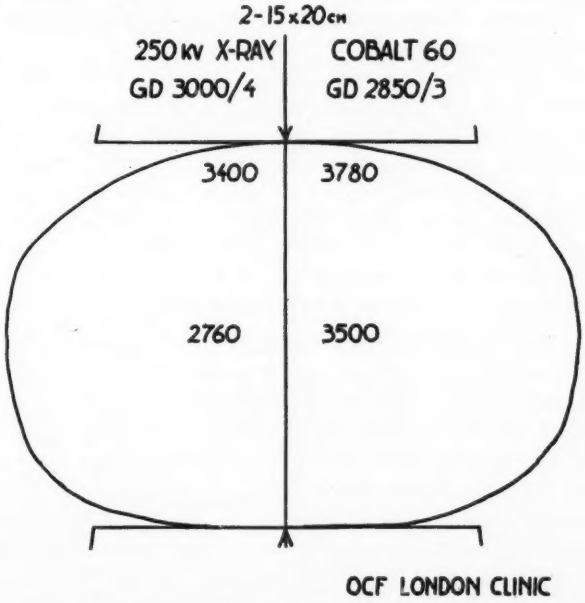

Fig. 1.—Treatment scheme for carcinoma of the ovary with the use of a pair of parallel opposed fields. Comparison is made of average maximum skin doses and central doses for x-ray therapy delivered in 4 weeks (left half), and cobalt^{60} delivered in 3 weeks (right half).

Table X records results in 52 ovarian malignancies, recurrent, residual, and postoperative, treated by cobalt^{60} from 1951 to 1953. Doctors and patients grasping at a straw in the early days of cobalt^{60} overloaded our case volume with advanced and recurrent cases. Even so, the over-all 3 to 5 year survival is 34.6 per cent, and the less advanced postoperative group it is 53.8 per cent.

The 53.8 per cent are all listed as "alive and well," which is more encouraging than the term "survival." As with any new therapeutic modality, experience adds safety and improvement, and we are settling into the second 5 year period of cobalt^{60} therapy with a continued spirit of clinical research and realism.

In such a spirit we are negotiating for a more serious consideration of the use of intraperitoneal radioactive gold prophylactically following operation in early cases. Our experience since 1951 in 86 cases of malignant peritoneal and pleural effusion has taught us to respect colloidal Au^{198}, as a palliative measure, really of value in one third and probably of some value in another third of all cases. At the present time, however, as a study in comparative effectiveness, we have switched to nitrogen mustard. To Hahn[11] we are indebted for radioactive colloidal gold and the reports from Zurich by Muller[12] in Stage I and II ovarian carcinoma are just too encouraging to dismiss. He reports Stage I as "the group in which a radical or seemingly radical operative removal of the tumor was possible," and of 19 cases followed up to 4½ years there was not a single recurrence. Muller's Stage II included cases where, "there were already pelvic tumor deposits beyond the ovaries, the removal of which was partially possible or even seemingly successful." Of 16 such patients 75 per cent remained free of symptoms one to 5½ years. These patients were treated postoperatively by radiogold, radium, and x-ray. With the attitude of public and profession attuned to early diagnosis, we should be prepared for such a radical approach in the earlier case.

Ordinarily we like the principle of bilateral oophorectomy and hysterectomy as the basis for dealing primarily with early ovarian cancer, but Kottmeier's[13] experience in leaving the uterus for radium insertion is quite intriguing and actually may prove advantageous for bulky fixed tumors or those associated with implants.

If, perchance, an ovarian carcinoma is deemed clinically inoperable, nothing will be lost, and, in some cases, much gained by preoperative irradiation. Indeed, at times, rather than scoop out a massive tumor, it is wiser to close the abdomen, irradiate, and tackle the problem surgically again at a later date.

Incidentally, granulosa-cell tumors are so radiosensitive that I question if ever they should be looked upon lightly. A 30 per cent recurrence rate in any other site is something we would fight to clear up. I submit that this is nearly possible with routine postoperative supervoltage. The following case history is illustrative of this tumor's radiocurability.

Case 52/1584.—This patient, aged 50 years, had a laparotomy in October, 1952, for removal of a cystic tumor of the right ovary. The uterus and left ovary had been removed several years previously. There were widespread intra-abdominal metastases. When she was seen for cobalt^{60} irradiation one month later, there was fullness in the pouch of Douglas, an ill-defined epigastric mass, and a diffuse mass on the right side extending from the costal margin to the crest of the ilium.

The entire abdomen was irradiated through 30 by 30 cm. anterior and posterior portals to a central tumor dose of 2,100 r in 3 weeks. When the patient was examined 4 years and 4 months later, there was no evidence of disease.

The problems of gynecological neoplasms constitute a major part of the activities of any organized cancer clinic, and we deem it most fortunate and significant that Canada's outstanding authority on gynecological cancer, Dr. W. G. Cosbie, is the Medical Director of the Ontario Cancer Foundation. He has the determination, skill, and fortitude of his Irish counterpart, Dr. Cullen, and the kindly tolerant touch of the master, Dr. Kelly. Under his wise judgment, stimulus, and leadership, we are making a determined effort to utilize

modern procedures fully in diagnosis and management, to carry our weight in clinical research, and to justify fully the trust that is placed in us by courageous patients and anxious families.

As compared with cancer in many other sites, cancer of the female genitals is mighty encouraging, particularly if one is selective in studying the 5 year cure rates recorded in early stages. A better appreciation and application of today's extended surgery, modern precise irradiation, and chemotherapy, and earlier diagnosis through education and exfoliative cytology will certainly brighten the colors for tomorrow's picture of gynecological cancer.

References

1. Paterson, R., and Parker, H. M.: Brit. J. Radiol. **7**: 592, 1934.
2. Tod, M. C., and Meredith, W. J.: Brit. J. Radiol. **11**: 809, 1938.
3. Heyman, J., editor: Annual Report on the Results of Radiotherapy in Carcinoma of the Uterine Cervix, 10th, 1954, and 7th, 1951, Stockholm, Sweden, Kungl. Boktryckeriet, P. A. Norstedt & Soner.
4. Smith, Ivan H.: J. Canad. A. Radiologists **3**: 16, 1952.
5. Thomson, D. H., and Smith, Ivan H.: J. Canad. A. Radiologists **8**: June, 1957.
6. Brunschwig, A.: Cancer **1**: 177, 1948.
7. Arneson, A. N., Stanbro, W. W., and Nolan, J. F.: AM. J. OBST. & GYNEC. **55**: 64, 1948.
8. Scheffey, L. C.: West. J. Surg. **60**: 144, 1952.
9. Cosbie, W. G., Anderson, W., Millar, O. B., and Bunker, M. L.: AM. J. OBST. & GYNEC. **67**: 1014, 1954.
10. Schmitz, H. E., Smith, C. J., and Gajewski, C. J.: AM. J. OBST. & GYNEC. **64**: 952, 1952.
11. Hahn, Paul F., editor: Therapeutic Use of Artificial Radioisotopes, New York, 1956, John Wiley & Sons, Inc.
12. Muller, J. H.: Peaceful Uses of Atomic Energy, Proceedings of the International Conference in Geneva, August, 1955, United Nations Publications, New York, vol. 10, pp. 110-114.
13. Kottmeier, H. L.: Carcinoma of the Female Genitalia, Baltimore, 1953, Williams & Wilkins Company.
14. Ontario Cancer Treatment and Research Foundation: Unpublished data.

RECTAL AND BLADDER INJURIES FOLLOWING RADIUM THERAPY FOR CARCINOMA OF THE CERVIX AT THE RADIUMHEMMET

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THE primary treatment of carcinoma of the cervix in Sweden has long been irradiation by the use of intracavitary radium application and external roentgen therapy. The treatment has been fractionated and, since 1924, has been individualized. The type of vaginal applicator used, the general condition of the patient, the degree of infection, and the position of the uterus have been some of the factors upon which this individualization was based.

In 1947 study was begun on the dosage distribution from various radium sources in the pelvis. Detailed measurements were carried out on 104 patients. Many of these were subjected to extraperitoneal lymphadenectomy according to the technique of Nathanson while the radium was still in place. Direct dosage measurements were made in various regions of the exposed pelvis with the use of a small ionization chamber. Special attention was directed toward ascertaining the separate distribution from the intrauterine and vaginal sources. In addition to readings along the ureters, the great vessels, the obturator nerve, and across the promontory of the sacrum, measurements were also made in the urinary bladder, the vagina, and the rectum. These findings were later confirmed by measurements on special phantoms constructed by Walstam.[1]

Beginning in January, 1949, an attempt was made to individualize treatment further according to the type and spread of the tumor, the width and elasticity of the vagina, and the distribution of radium dosage as found in the preceding studies. It soon became obvious that there was marked improvement in the primary results without any apparent increase in injuries. In a number of cases, however, the results were still unsatisfactory and Kottmeier therefore began to try various experimental techniques.

Extremely large intrauterine doses of radium were given to 2 patients with massive metastases in the lymph nodes on the lateral pelvic wall proved by biopsy to be carcinoma. Both patients were thought to have a hopeless prognosis, but both responded favorably. On postmortem examination 2½ and 4½ years later, no tumor could be demonstrated in the pelvis of either. One patient died of liver metastases and the other of coronary artery disease.

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Because of this unexpected result, the intrauterine dose was increased in certain selected cases. Two different methods were used: (1) applying the usual amount of radium for an increased length of time and (2) increasing the amount of radium applied in the uterine cavity to the range of 100 to 200 mg. In the latter cases, intrauterine applicators measuring 13 to 15 mm. in diameter were used. This technique was used chiefly in patients with paracervical spread, hydronephrosis, masses on the lateral pelvic wall, and other advanced lesions. It was found that primary healing occurred in some types of tumor in which it had not occurred previously.

By the end of 1952, however, there was a clinical impression that the number of radiation injuries had increased. The primary cure rate continued to improve and some very advanced lesions showed primary healing. It was decided that an attempt should be made to correlate rectal and bladder injuries with dosage distribution, but that until further data could be accumulated, the increased dosages should be continued. Actual measurements in the bladder and rectum were deemed necessary for each application because anatomical variation prevents the use of figures obtained on phantoms in the individual case.

Turner constructed a dosimeter which could be placed in the bladder and rectum and this was applied clinically by Lederman and Lamberton.[2] The Bomke-Eberle dosimeter was highly recommended[3] but had the disadvantage of requiring a long time for readings. Sievert and Walstam, therefore, worked out a modification of Turner's apparatus utilizing a 0.3 c.c. Sievert ionization chamber in a probe which could be introduced into the bladder and rectum. Measurements with this instrument were started in July, 1953. Treatment was not modified on the basis of the readings obtained so that an attempt could be made to discover under which conditions injuries occurred most frequently.

The following is a preliminary report attempting to correlate injuries with an objective measurement of the dose in roentgens delivered to the mucosa of the bladder and rectum and with the size and intensity of the intrauterine radium application.

Material

Five hundred consecutive cases of invasive carcinoma of the cervix treated at the Radiumhemmet from July, 1953, to September, 1954, were reviewed. All patients were followed from one to three years. The distribution of the cases according to the International classification was:

Stage I	17.2%
Stage II	61.2%
Stage III	18.0%
Stage IV	4.2%

A carcinoma fixed to the pelvic wall by a firm but not nodular parametrium has been designated Stage II. In general we have required a positive biopsy to classify a growth as Stage IV.

Essentially complete physical measurements of radiation dosage to bladder and rectum were available for only 369 of these, but all 500 were studied for injuries. The patients were treated according to the current modification of the "Stockholm technique" which stresses individualization of cases.

Measurements were made with an ionization chamber contained in a curved probe which could be covered by a sterile rubber sheath. The instrument was calibrated in gamma roentgens per hour and under the conditions of clinical use had an accuracy of ± 10 per cent in the range of 20 to 180 r per hour. It was checked at regular intervals by the department of radiophysics.

Immediately after the insertion of radium and packing of the vagina, with the patient under anesthesia and in the lithotomy position, the probe was inserted in the bladder to a depth of 10 to 12 cm. With the probe in the midline and with gentle pressure downward, it was slowly withdrawn and the dosage rate at each centimeter of distance recorded. The chamber was then inserted 12 cm. into the rectum and similar measurements recorded along the anterior rectal wall. The point of maximum radiation in the rectum varied from 4 to 12 cm. above the anus and could not be correlated with the type of vaginal applicator used. Even greater variation was found in the bladder. In the calculations which follow, the measurements at 7 and 10 cm. have been used.

Results

In the initial review of the cases, *all* symptoms relating to bladder and bowel were noted, but minor degrees of cystitis and proctitis during the actual period of radiotherapy were both common and transient and could in no way be correlated with later symptoms. These have not been analyzed further.

For this paper, bladder and rectal injuries have been divided into three groups. The Grade 1 injuries are those producing mild subjective symptoms after the completion of therapy but minimal or no objective changes and also those minor objective changes in the mucosa which were asymptomatic. These are really radiation *reactions* and not injuries. The second group is composed of the moderately severe objective injuries such as ulcers, slight stenoses, or bleeding, which, though frequently short lived, are distressing to the patient. The third group is made up of the cases of fistulas and those rectal stenoses requiring colostomies. This third group is presented in detail below. Fistulas occurring within one month after electroendothermy for recurrent or radioresistant disease[4] were considered to be due to the fulguration and were excluded from the present study, as were the majority of fistulas arising in the terminal stages of patients who died of cancer. There were no small bowel injuries or deaths attributable to radiation injuries. There was one immediate death due to peritonitis.

Fifty-five, or 11 per cent, of the patients had symptoms related to the urinary tract following the completion of their radiotherapy and have been classified as having Grade 1 bladder injuries. Many of these symptoms may have been due to infections of the urinary tract, but cultures were not obtained in all cases.

There were 9 patients, or 1.8 per cent, whose bladder injuries were placed in the second group. Six of these had ulcers or areas of necrosis seen on cystoscopy and 3 had symptoms of prolonged cystitis with minimal objective changes. Three patients developed vesicovaginal fistulas and were placed in the third group. Two of these were patients with late Stage III lesions and the other had a Stage IV tumor with bladder invasion. Two of the 3 eventually died of their disease, but the time interval was such that the fistulas could not be considered strictly terminal phenomena.

Eighty-six, or 17 per cent, of the patients were classified as having Grade 1 injuries of the rectum. All of these were transitory. Thirty-one, or 6.2 per cent, were grouped as showing Grade 2 rectal injuries. The signs and symptoms of this group are analyzed in Table I. Ten had slight-to-moderate strictures of the rectum or rectosigmoid, 2 had ulcers of the rectal mucosa, and 2 had anemia

secondary to rectal bleeding severe enough to require transfusion. Seventeen of the 31 became asymptomatic during the period of observation and 6 died of their disease. Classified as Grade 3 injuries were 6 rectovaginal fistulas and 2 rectal stenoses requiring colostomies.

TABLE I. SIGNS AND SYMPTOMS OF GRADE 2 RECTAL INJURIES, 31 CASES

Signs.—	
Rectal edema	18
Stenosis of rectum	8
Stenosis of sigmoid	2
Rectal ulcer	2
Anemia, marked	2
Fever	2
Symptoms.—	
Rectal bleeding	23
Rectal pain	12
Mucus	10
Tenesmus	9
Diarrhea	6

Since the number of Grade 3 injuries was too small for statistical analysis, the Grade 2 and 3 injuries have been lumped together in many of the tables as injuries considered "serious" at the Radiumhemmet.

Brief summaries of the cases with Grade 3 rectal and bladder injuries follow:

CASE 1.—E. O. was a 59-year-old para 0 who had a Stage IV lesion with bladder invasion, a large rectal mass, and extension to both pelvic walls. Initial radium treatment consisted of 150 mg. for 20 hours in the uterus followed 2 months later by 70 mg. for 30 hours in a curved vaginal box. Between these treatments she received 3,400 r skin dose with a 200 kv. x-ray machine to one 15 by 18 cm. abdominal field and a similar posterior field. Six months later a positive biopsy was obtained from a large mass on the right pelvic wall and she developed pain in the right side. The case was considered hopeless, but she was re-treated with 180 mg. of radium for 25 hours placed directly into the tumor mass on the pelvic wall and with 1,400 r additional x-ray therapy. Six months after this she was found to have rectovaginal and vesicovaginal fistulas. The patient died of carcinoma with metastases 26 months after her initial treatment. No radiation measurements were obtained on this patient.

CASE 2.—J. B. was a 64-year-old para iv with a Stage III carcinoma who complained of hematuria but did not have biopsy-proved bladder invasion. Because of a previous perforation of the uterus, no radium was placed in the uterus initially and her first treatment consisted of 150 mg. of radium in a long narrow vaginal cylinder for 12 hours. This was followed in 4 weeks by 62 mg. in the uterine cavity for 25 hours and 100 mg. in a short, thick vaginal cylinder for 20 hours, a greatly increased vaginal dose by Stockholm standards. No dosage measurements were made. External radiation consisted of 2,000 r to each of two perineal ports, 2,400 r to one large posterior field, and an additional 1,200 r to a field in the right lower quadrant. Six weeks later an electrofulguration was done because of persistent tumor. Six months after this the patient was found to have a vesicovaginal fistula, followed by a rectovaginal fistula 6 months later. A colostomy was performed and 31 months after her original treatment she was clinically free of tumor.

CASE 3.—A. N., a 70-year-old para ii, was found to have a Stage III carcinoma of the cervix in addition to a far-advanced carcinoma of the breast. She was given 64 mg. of radium in the uterus and 70 mg. in a curved vaginal box for 27 hours at the time of first treatment, followed by 200 mg. for 17 hours in the uterus 3 weeks later. Measures were obtained showing that she received a dose of more than 7,930 gamma r in the bladder and 2,915 gamma r in the rectum. She received 2,000 r to each of four fields by x-ray. Four

months after treatment she was found to have a vesicovaginal fistula and rectal stenosis. She died immediately thereafter. Although this fistula was, in a sense, terminal, it was felt that in view of the dosage given to the bladder it must be included with the radiation injuries.

CASE 4.—I. A., a 64-year-old para v, was classified as having a late Stage II lesion. She received an increased intrauterine dose of 180 mg. of radium for 20 hours and 70 mg. of radium for 25 hours intravaginally in a large curved box. The uterus was perforated and she developed pelvic peritonitis. Three weeks later she received 55 mg. in the uterus and 70 mg. in the vagina for 25 hours. A pelvic abscess developed which drained by perforation into the sigmoid. Measurements were incomplete but indicated a high rectal dose. External radiation consisted of 2,400 r to each of 4 fields, 2 anterior and 2 posterior, and 1,600 r to one vulvar field. Nine months later she developed a fistula from the sigmoid to the corpus. Ten months after this the fistula had spontaneously closed. The patient was alive and well 2½ years after treatment.

CASE 5.—H. J. was a 52-year-old para i with a late Stage II carcinoma. She received an increased intrauterine dose of 200 mg. of radium for 20 hours at the time of the first treatment, followed in 4 weeks by 53 mg. in the uterus and 70 mg. in two ovoidlike capsules in the vagina. X-ray therapy consisted of 2,000 r to each of six fields; two perineal, two anterior abdominal, and two posterior. The total dose in the rectum was 7,145 r and the dose in the bladder was 2,540 gamma r. One year after treatment she developed pain on defecation and tenesmus, followed 2 months later by a rectal ulcer. Two months after this a colostomy was made because of a rectovaginal fistula. She has now lived for more than a year with proved recurrent carcinoma in the bladder.

CASE 6.—M. O., a 59-year-old para v with diabetes, had a late Stage II lesion involving the upper half of the posterior wall of the vagina. She was treated with 74 mg. of radium in an intrauterine tandem and 70 mg. in the vagina for 25½ hours, followed in one month by 66 mg. in the uterus and 70 mg. in the vagina for 27 hours. Because of a narrow vagina, small capsules were placed in the vagina instead of the more commonly used boxes. External radiotherapy was stopped after 800 r because of leukopenia. Measurements showed a dose of 6,060 gamma r to the rectum and 3,120 gamma r to the bladder. Four months after treatment she noted rectal bleeding which became persistent and severe. Four months later she developed a rectal ulcer and six months after this was noted to have a small rectovaginal fistula. This patient required 30 blood transfusions, because of rectal bleeding. She died of a primary carcinoma of the stomach. No tumor was found in the pelvis on autopsy.

CASE 7.—K. K., a 58-year-old para i, was classified as having a Stage III lesion because of extension down two-thirds of the posterior vaginal wall. It was noted that the extent of the lesion resembled that of a primary carcinoma of the vagina. She received 64 mg. of radium in the uterus and 80 in the vagina for 27 hours at the first treatment and 64 and 70 mg. for 25 hours at the second. The vaginal boxes were tamponaded against the tumor on the posterior vaginal wall. She received 2,000 r to each of six ports, two perineal, two abdominal, and two posterior. Measurements showed that she received a dose of 7,445 gamma r to the rectal mucosa and 4,791 to the bladder. Four months after treatment she began to have rectal symptoms consisting of tenesmus, bleeding, and pain. During the next 4 months the rectal lesion progressed to stenosis and fistula, and the patient died with persistent disease. The fistula was probably due to disease, but in view of the high dose given to the rectum the case is included with the rectal injuries.

CASE 8.—G. K., a 45-year-old patient, had an extensive exfoliating Stage II carcinoma involving the upper half of the posterior wall of the vagina. Her initial treatment consisted of 183 mg. of radium in the uterus for 22 hours followed by 70 mg. of radium in the vagina in a flat box for 27 hours. At the second treatment she was given 66 mg. in the uterus and 70 mg. in the vagina for 25 hours. Six weeks after this seven 20 mg. radium

needles were inserted into the area of the left uterosacral ligament for 8 hours. She received 2,000 r to each of two perineal ports, 1,600 r to the right anterior and posterior ports, and 2,800 r to the left. The rectal dose excluding that from the radium needles was 6,132 r, the bladder dose, 4,380. Three months after treatment she began to pass blood and mucus in the stool. Shortly after this she developed rectal stenosis and ileus, and a colostomy was made. After 20 months, she had no evidence of progressive disease, but the colostomy was still required.

CASE 9.—M. L. was a 32-year-old para i who had had a previous myomectomy and presented with a Stage II carcinoma of the cervix. She was treated with 150 mg. of radium in the uterus and 70 mg. in the vagina for 25½ hours, an increased intrauterine dose. Three weeks later she received 64 mg. in the uterus and 70 mg. in the vagina for 25 hours. The bladder dose was measured as 5,460 gamma r and the rectal dose as 2,520 gamma r. The first course of external radiotherapy consisted of 200 r to each of two anterior and two posterior fields, followed by 400 r teleradium to two left inguinal fields. Because of pain, 40 mc. of radioactive gold was injected into the left parametrium and 30 mc. into the right. The pain improved but recurred six months later at which time she was given additional treatment using telecobalt. Four months after this she developed left lower quadrant pain and was found to have stenosis of the rectum and necrosis of the colon. A colostomy was made at the time. She died of disease 3 months later.

The factors responsible for the fistulas are clear in many of these cases. Numbers 1, 3, 5, and 7 were essentially terminal fistulas due to disease, but because of the long intervals between the development of the fistulas and death, have been included with the injuries. In Cases 1, 3, 7, and 8, tumor was present in the rectovaginal septum and radium was deliberately packed against the tumor even though the risk of injury was known to be high. Three of the cases (1, 8, and 9) were treated experimentally with the use of additional radium, radium needles, radioactive gold, and external therapy with $Cobalt^{60}$ in an attempt at palliation. The experiences with gold have been reported elsewhere.[5] In Cases 2 and 4, the treatment was modified because of perforation of the uterus; the latter patient developed her fistula through the tract of drainage of a pelvic abscess secondary to the perforation.

Thus there were very few fistulas in the cases which were treated with a more or less standard technique and which went on to healing of the primary lesions. The other cases have been included to point out the problems encountered in treating far-advanced and recurrent disease.

Correlation

The injuries included in this series have been analyzed in Table II according to the stage of tumor treated. There were no fistulas among patients with Stage I lesions. In general there were increasing numbers and severity of injuries with increasing stage. In Table III the cases have been regrouped into early and late lesions, the former consisting of the Stage I and Stage IIA tumors. The difference in injury rate is found to be statistically significant when the cases are divided in this way.

Table IV correlates rectal injuries with the dose measured in the rectum at the time of radium insertion. With increasing radiation, there is a gradual increase in the rate of serious injuries. Above 5,000 gamma r this becomes 18.5 per cent of the cases treated. If the radiation received by the rectum from external therapy given with a 200 kv. machine is added to the dose from the radium, the *total* number of roentgens received by the rectum can be correlated with injuries (Table V). There is an abrupt increase in injuries when the *total* dosage is over 6,000 r with a rate of 15.3 per cent serious injuries compared to a rate of 4.2 per cent when the total dosage is less than 6,000 r.

TABLE II. RECTAL AND BLADDER RADIATION INJURIES ACCORDING TO THE INTERNATIONAL CLASSIFICATION OF CARCINOMA OF THE CERVIX

GRADE OF INJURY	STAGE I (%)	STAGE II (%)	STAGE III (%)	STAGE IV (%)	ALL STAGES (%)
Bladder.—					
1	7.0	11.9	12.2	9.5	11.2
2	2.3	1.3	2.2	4.7	1.7
3	0.0	0.0	2.2	4.7	0.6
Rectum.—					
1	16.3	16.2	26.7	4.7	17.4
2	1.2	8.6	6.9	0.0	7.0
3	0.0	2.0	2.2	4.7	1.8

TABLE III. RATES OF SERIOUS INJURIES (GRADES 2 AND 3) IN EARLY LESIONS COMPARED TO LATE LESIONS

STAGE	NO. OF CASES	BLADDER INJURIES	RECTAL INJURIES
I and IIA	204	1.0%	3.9%
IIB, III, and IV	261	2.7%	9.6%

TABLE IV. CORRELATION OF RECTAL INJURIES WITH DOSAGE IN GAMMA ROENTGENS MEASURED IN THE RECTUM

GAMMA R	NO. OF CASES	GRADE 1 (%)	GRADES 2 AND 3 (%)
0-1,999	19	10.6	5.3
2,000-2,999	81	12.2	2.5
3,000-3,999	116	18.1	6.9
4,000-4,999	66	19.7	10.6
5,000-5,999	44	22.7	18.2
6,000 and over	10	20.0	20.2

TABLE V. CORRELATION OF RECTAL INJURIES WITH TOTAL DOSAGE OF RADIATION RECEIVED FROM RADIUM AND EXTERNAL RADIOTHERAPY

TOTAL R	NO. OF CASES	GRADE 1 (%)	GRADES 2 AND 3 (%)
0-3,999	41	12.1	0.0
4,000-4,999	82	12.2	4.9
5,000-5,999	87	16.0	5.7
6,000-6,999	70	28.6	14.2
7,000-7,999	35	17.1	14.2
8,000 and over	19	15.8	21.1

TABLE VI. INJURY RATE (GRADES 2 AND 3) AFTER ROUTINE STOCKHOLM TREATMENT COMPARED WITH THE RATE AFTER AN INCREASED INTRAUTERINE TREATMENT IN 268 STAGE II CARCINOMAS OF THE CERVIX

	NO. OF CASES	BLADDER INJURIES	RECTAL INJURIES
Routine treatment	190	1.8%	6.7%
Increased intrauterine treatment	78	0.0	20.5%

TABLE VII. CORRELATION OF GRADE 2 AND 3 RECTAL INJURIES WITH INTENSITY OF TREATMENT

GAMMA R PER SINGLE TREATMENT	DURATION OF TREATMENT	
	24-30 HOURS	15-22 HOURS
2,500-2,999	6.0%	16.6%
3,000+	12.1%	30.0%

Within the dose range studied, there was very little correlation between bladder injuries and the measured dose of radiation. There was a rise in severe bladder injuries when the bladder mucosa received more than 7,000 r, but this group was too small for any definite conclusion to be drawn.

One of the objects of this study was to discover the specific effect of increasing the intrauterine dose on the incidence of radiation injuries. This was studied in 168 cases of Stage II lesions. The results are given in Table VI. There appeared to be no effect on the bladder, but the increase in rectal injuries is statistically significant.

It has long been maintained that there is a relationship between injuries and intensity (radiation per unit time). Table VII shows that the patients who received more than 2,500 gamma r in a single treatment developed serious rectal injuries 2½ times as often when the treatment was given in less than 22 hours than when it was given in 24 hours or more. The difference is statistically significant.

An attempt was made to determine the relationship of serious rectal injuries to other factors of possible etiological significance, such as the presence of pelvic adhesions and retroversion of the uterus. The injury rate in patients with a history of salpingitis and those whose temperatures spiked above 38.5° C. during treatment did not differ significantly from the mean. In 50 patients with a history of previous pelvic surgery, it was 16 per cent compared with an average of 8.8 per cent. This is of borderline significance. The rate in women with retroflexion of the uterus was only 6.6 per cent, but the intrauterine dose was decreased in such patients in order to prevent rectal injury. There were only 14 cases of carcinoma of the cervical stump and no serious injuries occurred in this group.

Parity was recorded in all cases but did not appear to be significant. No correlation could be found with the type or size of vaginal applicator used except in women with very narrow vaginas when the usual Stockholm boxes were replaced in both treatments by a single vaginal cylinder or by a pair of small vaginal capsules. Under these conditions, the incidence of serious rectal injuries jumped to 15 and 24 per cent, respectively.

Comment

In 1932 Sievert[6] reported a series of measurements of radiation received by the rectal mucosa during treatment of carcinoma of the cervix which he obtained by the use of ionization chambers. He studied the distribution of radiation from different types of radium applications but made no attempt to correlate these with rectal injuries. With the development of more practical dosage meters in the past ten years, numerous investigators, including Deeley,[7] Fletcher,[8] Lederman,[2] Ries,[3] Strickland,[9] and Zilliacus,[10] have tried to make such a correlation. The conclusions as to the critical level of rectal radiation vary from 3,300 r to 8,000 r. These figures relate to series of patients treated under many different systems and, therefore, each applies only to the specific conditions studied. The levels above which there was an increase in rectal injuries in the present series were 5,000 gamma r and 6,000 total r.

One of the variables which seems to be of importance in determining the amount of radiation that the rectum will tolerate is the intensity of the treatment. In this group of patients, among those who received a comparable increased intrauterine dose, decreasing the time of treatment from 24 to 30 hours

to 22 hours or less was accompanied by an increase in the incidence of rectal injuries from 9.3 to 22.7 per cent. The survival rate in the group who received a large intense dose of radium and developed severe rectal injuries was somewhat higher than in the series as a whole even though all of these patients had advanced lesions. This is similar to the results reported by Ingelman-Sundberg,[11] but the group is too small for any definite conclusions to be drawn.

The other factor which seems to be of importance in the etiology of rectal injuries is the width of the vagina, as borne out by the large number of rectal injuries in women in whom only narrow vaginal applicators could be fitted. There was no correlation with age.

Factors commonly thought to contribute to rectal injuries but not accompanied by a high incidence of these in this series include retroversion of the uterus, presence of a cervical stump lesion, and febrile response to radium. The importance of these factors was not *disprove* by this study because, at the Radiumhemmet, the total dose of radiation given is usually decreased under these conditions.

The patients have not been followed long enough for all reactions to have developed. Hollstein[12] found that 80 per cent of bladder reactions occur within one year of treatment and Gauwerky,[13] Bonebrake,[14] and Gardner[15] report that almost all large bowel lesions occur in the first year. Since all of these patients were followed one to three years, the majority of serious injuries should have been detected.

If the 5 year apparent recovery rates for the years 1949 to 1952 are compared with those of 1936 to 1945 (Table VIII), there has been improvement in the various stages and in the total survival rate. With this there has been an increase in radiation injuries, especially in patients treated experimentally who received larger and more intense intrauterine radium doses. Since few of these injuries have had permanent sequelae, and the fistula rate is still low compared to that of many other institutions, a small increase in the number of injuries may be justified. Similar increases in radiation injuries in conjunction with increased radiation dosage and increased survival rates have been reported by Porter,[16] Lewis,[17] and Brack.[18]

TABLE VIII. FIVE-YEAR APPARENT RECOVERY RATES FOR THE YEARS 1949 TO 1951 COMPARED WITH THE APPARENT RECOVERY RATES FROM 1936 TO 1945

	1936-1945		1949-1951	
STAGE	NO. OF PATIENTS TREATED	5 YEAR APPARENT RECOVERY RATE (%)	NO. OF PATIENTS TREATED	5 YEAR APPARENT RECOVERY RATE (%)
I	299	69.2	155	89.0
II	1,440	51.4	605	54.5
III	787	24.4	230	33.5
IV	230	11.3	91	7.8
I-IV	2,756	42.3	1,081	51.1

All unnecessary injuries should be avoided. In the past year at the Radiumhemmet, treatment has been modified on the basis of the data analyzed here and on the basis of measurements of the radiation dosage rate in the bladder and

rectum at the time of the insertion of radium. This has been accompanied by a reduction in the number of radiation injuries. This study shows, however, that all injuries cannot be prevented in this way.

Conclusions

1. The experimental use of highly individualized treatment of carcinoma of the cervix with an increased intrauterine dose in the advanced lesions has been responsible for increased survival rates, but has necessitated a re-evaluation of radiation injuries.

2. There is a correlation between both radium dosage and total radiation received by the rectum and the incidence of rectal injuries. A dose of more than 5,000 gamma r or 6,000 total r appears to carry a high risk of injury.

3. A significant increase in rectal injuries with increased intensity of radium treatment was demonstrated. A dose of 2,400 r to the rectum in 24 hours is the maximum which should be used.

4. A narrow vagina as reflected by the type of radium applicator which could be accommodated was also a factor of significance in increasing the probability of rectal injuries.

5. Some rectal and bladder injuries can be prevented by the routine use of a dosage meter in the bladder and rectum at the time of insertion of radium to pick out the cases receiving an unusually high dose and re-evaluate the application in the individual case.

6. This series should be regarded as an experimental study and does not reflect the current rate of radiation injuries at the Radiumhemmet. Some of the fistulas included were actually terminal phenomena or due to planned over-irradiation.

References

1. Walstam, R.: Acta radiol. **42**: 237, 1954.
2. Lederman, M.: Brit. J. Radiol. **23**: 430, 1950.
3. Ries, J.: Strahlentherapie **82**: 23, 1950.
4. Kottmeier, Hans L.: In Meigs, J. V., editor: Surgical Treatment of Cancer of the Cervix, New York, 1954, Grune & Stratton, Inc., p. 412.
5. Kottmeier, H. L., and Moberger, G.: Acta obst. et gynec. scandinav. **34**: 1, 1955.
6. Sievert, R. M.: Acta radiol., supp. 14, pp. 1-179, 1932.
7. Deeley, T. J.: J. Fac. Radiologists **5**: 289, 1954.
8. Fletcher, G. H.: Radiology **60**: 77, 1953.
9. Strickland, Paul: Brit. J. Radiol. **27**: 630, 1954.
10. Zilliacus, Harry: Acta radiol. **28**: 790, 1947.
11. Ingelman-Sundberg, A.: Acta radiol., supp. 64, pp. 1-79, 1947.
12. Hollstein, K., and Hess, M.: Strahlentherapie **87**: 295, 1952.
13. Gauwerky, F.: Strahlentherapie **80**: 51, 1949.
14. Bonebrake, M. D., and Sherman, A. I.: J. Missouri M. A. **49**: 19, 1952.
15. Gardner, C. E., and Anlyyan, W. G.: Surgery **31**: 746, 1952.
16. Porter, E. C., and Sycamore, L. K.: Radiology **59**: 103, 1952.
17. Lewis, Geo. C., Chamberlain, R. H., Hale, John, and Payne, F. L.: Am. J. Roentgenol. **72**: 975, 1954.
18. Brack, C. B., Everett, H. S., and Dickson, R.: Obst. & Gynec. **7**: 196, 1956.

DOUBLE CARCINOMA OF THE CERVIX*

Case Report

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I WISH to report a case of double carcinoma of the cervix.

This patient is a gravida ii, para ii, aged 56 years. She had had negative cervical biopies in November, 1955, and smears were made from the vagina in October, 1956, and were reported negative, but biopsies were requested. Dr. Paul Laube of Dubuque, Iowa, made multiple cervical biopsies and the pathologist then made a diagnosis of adenocarcinoma. This patient never had any bloody show or pain, but did have increased vaginal discharge. She came under observation because of two recent attacks of cystitis.

On Dec. 18, 1956, when I removed the uterus by radical hysterectomy and wide cuff section, it was found that she had both adenocarcinoma and squamous-cell carcinoma coming within a few millimeters of each other. In a few places there was some invasion of the basement membrane by the squamous-cell carcinoma, but 10 hypogastric and other lymph glands taken from the side on which the growth occurred were all negative. She has, however, been followed with deep x-ray therapy. The pathologist's report was as follows:

1. Adenocarcinoma of the cervix and squamous-cell carcinoma of the cervix with 10 negative left hypogastric nodes.
2. Early atrophy of the endometrium.
3. Leiomyomas of the uterus.
4. Two ovaries and Fallopian tubes.

Following her x-ray treatments she spent the winter in Florida and on March 28, 1957, her weight was 127, the most she had ever weighed in her life. The blood pressure was 116; the abdomen normal and soft; vaginal pH 4.5; and vagina well healed. She reported normal orgasm. A Papanicolaou smear at that time was normal, urine normal, sedimentation rate 14 mm. in 60 minutes, hematocrit 43, hemoglobin 94 per cent, erythrocyte count 4.62 million, leukocyte count 4,450, neutrophils 58, lymphocytes 40, eosinophils 2.

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*Presented at a meeting of the Chicago Gynecological Society, May 17, 1957.

UROLOGICAL ASPECTS OF GYNECOLOGY*

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(From the Department of Gynecology, the Johns Hopkins University)

I CAN think of no better way of commemorating the name of Joseph Baer than by a memorial lecture. In addition to his talents as a gynecologist and obstetrician, he had a gift for speaking far in excess of that of the average medical man. His thoughts were logical, and his diction was particularly clear. When he had finished speaking at a scientific meeting, there was left no doubt as to exactly what he thought about the subject at hand. I was born into the gynecological world at the time when Joseph Baer was at the acme of his medical career. To listen to him present his subject was a lesson to us younger men and a real challenge to those of us who were to follow him. I am grateful and proud of having been selected to give this memorial lecture.

On such an occasion as this, it is fitting to select a subject which, in some way, is related to the interests of the man in whose memory the lecture is given. That Dr. Baer was interested in the urological aspects of gynecology is attested by the subject he selected for his presidential address before the American Gynecological Society in 1950. He spoke then upon the life of J. Marion Sims, the father of surgery of vesicovaginal fistula in this country. Since Dr. Baer's heyday, female urology has assumed a more important place in gynecology and obstetrics.

I happen to have fallen heir to a department of gynecology in which, from its inception, urology has been an integrated part. From the time of Howard Kelly's assuming the chair of gynecology at the Johns Hopkins, he apparently took it for granted that the urinary tract was part of his domain. His invention of the Kelly air cystoscope was somewhat accidental. He had been working for some time at visualizing the female bladder through a simple speculum with a glass window with the patient in the knee-chest position. By accident, the window was broken out of one of these specula, and the broken speculum was, by chance, placed on the instrument table. Dr. Kelly asked the nurse for a speculum, and the one without a window was handed him. When it was passed into the bladder of the woman in the knee-chest position, the bladder sucked in air and ballooned out. Kelly thus visualized the interior of the bladder through a cystoscope and through the medium of air for the first time, and passed a catheter up a ureter under direct vision. This is but one of many examples of the prepared mind seizing the advantage of an accidental opportunity.

*The Seventh Joseph L. Baer Lecture, presented at a meeting of the Chicago Gynecological Society, Oct. 19, 1956.

Our female urology obtained further impetus by the accident of World War II. It so happened that when the Hopkins Hospital units were formed there were no urologists available, and the positions of urologists were filled by gynecologists from our department. A quick textbook review of the male genital apparatus apparently satisfied army requirements. One of these "gynecological urologists" went so far as to remove the prostate of a native chieftan in the Fiji Islands. As a reward for this successful operation, he was made honorary chieftan of the tribe. In spite of this digression from gynecology and his acceptance of male patients, he was subsequently certified by the American Board of Obstetrics and Gynecology. This experience made these men adept with the water cystoscope as well as the air method of cystoscopy, and all of our residents since the war have become proficient in both methods.

In the time at my disposal this evening, I shall attempt to review our experiences in urology as applied to gynecology. It will become obvious to you that much of what I have to report tonight is the work of my colleagues in our department. After starting to put my thoughts together for this occasion, I came to the realization that the subject is too comprehensive to cover in a single lecture. I therefore have had to omit important phases of the subject, such as vesicovaginal fistula, and will confine my talk to some of the other facets of the subject in which our clinic has been particularly interested.

I shall first have a few words to say about urinary tract infections in gynecology. In taking urological histories in women, I am struck with the fact that, in a goodly percentage of the cases, the initial attack of urinary tract infection occurred during pregnancy, during the puerperium, or during the immediate postoperative period. A small percentage of these infections, which are often initially limited to the bladder, eventually involve the kidneys. Sometimes the kidney infection is transient but it *may* result in chronic pyelonephritis and this disease kills more people than any other type of kidney disease. It therefore behooves us as gynecologists and obstetricians, first, to prevent urinary tract infections, if possible, and, second, to clear up completely the infection which originated while the patient was under our care.

That the proper care of the urinary bladder postoperatively is important in preventing infection was emphasized by the late Arthur Curtis. This consists in catheterization at intervals, if there is any reason to believe the patient is not completely emptying her bladder. Once having been catheterized, the importance of catheterization for residual urine should be stressed until the residual is less than 100 c.c. A running stream remains clear; algae thrive in the mill pond. So it is with propagation of bacteria in the stagnant residual urine.

How do we know that infection originating in the bladder may ascend into the kidneys, and what is the mechanism by which this occurs? We have some clinical evidence, presented by the postoperative patient, who, after several afebrile days with symptoms of cystitis, suddenly develops fever with symptoms of pyelitis. With normal valve action at the ureterovesical junction, it is unlikely that retrograde infection very often travels up to the kidney via

the ureteral lumen. It is our belief that the usual modus operandi is via the periureteral lymphatics. That such lymphatic drainage does occur was demonstrated more or less accidentally in our recent experimental work on endometriosis. One of our monkeys, which developed a mass of endometriosis near the lower end of the ureter, died. Autopsy showed healthy-looking endometrium growing in that kidney, obviously a lymphatic transplant from the mass of endometrium surrounding the lower end of the ureter.

The proper use of the catheter is important when we have postoperative retention, but it is better to *prevent* the necessity of catheterization, if possible. This we have accomplished in a great measure in our laparotomies by instilling an ounce of 0.5 per cent aqueous solution of Mercurochrome into the bladder in the operating room while the patient is still asleep. Woodruff and I have shown that, by carrying out this simple procedure, only 6.5 per cent of our laparotomized patients required catheterization one or more times, while in a control series, 51 per cent required catheterization. Moreover, the patients who had the instillation voided earlier and more nearly completely emptied their bladders.

With simple vaginal hysterectomy and early ambulation, catheterization is not often necessary, but when plastic work has been done on the anterior vaginal wall, spontaneous voiding immediately postoperatively is rare. We have found the Mercurochrome instillation of no value in these cases, and we believe an indwelling catheter for four days is advisable.

In spite of all precautionary measures, postoperative urinary tract infection remains the commonest postoperative complication. When it occurs, it should be treated immediately and thoroughly until the urine is sterile. The organisms should be isolated and tested for sensitivity to the various antibiotics for possible later use. Since the most frequent organism is coli-aerogenes, sulfonamide therapy should be started immediately. Gantrisin is very soluble and avoids the dangers of crystalluria. Everett and Long have shown that this therapy, if carried out with sufficient dosage, usually successfully clears up the simple forms of infection and they recommend that antibiotic therapy, selected by means of sensitivity tests, be reserved for those organisms which prove resistant to sulfonamide therapy.

Before leaving the subject of urinary tract infection, there is one more point which I wish to make. There are certain cases of persistent *Escherichia coli* infection of the urinary tract which fail to respond to the usual sulfonamide therapy. Everett, Scott, and Steptoe showed that succinylsulfathiazole administered in daily doses of 0.125 Gm. per kilogram of body weight for two weeks may be effective in eradicating the infection. Later Everett, Davis, and Vosberg showed that equally good results could be obtained with Sulfathalidine with much smaller dosage. These sulfonamides are absorbed into the blood stream scantily, and their primary action appears to be on the intestinal flora. The most probable mode of action seems to be the elimination of the source of infections from the bowel, permitting the urinary tract to throw off infection by means of its resistant powers. These drugs, in our hands, have proved ineffective against infections due to organisms other than *E. coli.*

In connection with persistent pyuria, there are two conditions which should always be kept in mind. Benign urethral polyps, most frequently in the posterior urethra, are usually infected. Their destruction by fulguration generally results in the clearing up of the infection. Urethral diverticulum may also be responsible for persistent bladder infection. In spite of the fact that Hey described the abnormality as far back as 1805, it is today a greatly neglected condition. It seems apparent that whenever it is called to the attention of the profession in the literature more cases are diagnosed. Then, after a lapse of time, the condition seems to be overlooked again. This point is well illustrated by our own experience. During the 19 year period, 1931-1949, 22 cases were diagnosed and treated by us. These cases were reported by Wharton and Kearns in 1950. In the succeeding 5 years, 41 cases were diagnosed.

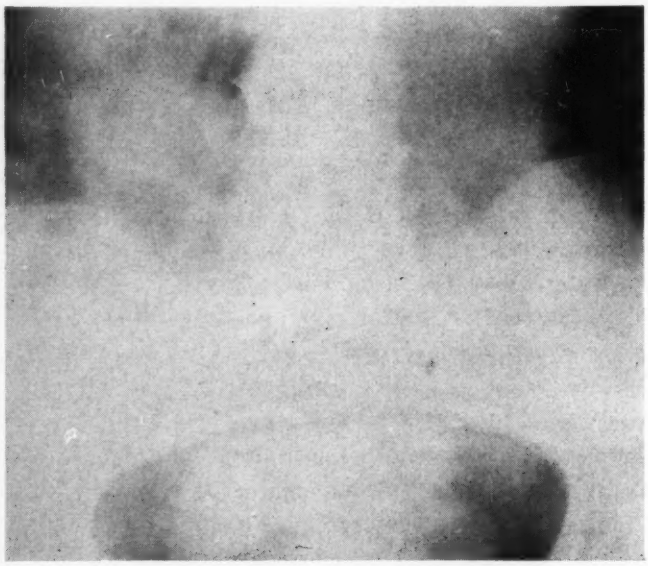

Fig. 1.—X-ray visualization of urethral diverticulum.

These 63 cases were studied and reported by Wharton, Jr., and me. Now that our entire staff has been alerted, a case appears every week or two. The symptomatology is essentially that of recurring chronic cystitis, and the common story is that of a woman who has been repeatedly cystoscoped and treated for chronic urinary tract disease without permanent relief. There are other specific symptoms and signs which are present in some cases, such as acute retention, the appearance of a suburethral mass, the appearance of pus at the urethral meatus on stripping the urethra, and stress incontinence. The methods of diagnosis consist of palpating the mass, expressing pus from the urethra, visualizing the opening into the urethra by cystoscopic methods, and the demonstration of the cavity by means of x-ray visualization. Fig. 1 shows such a visualization and Fig. 2 shows a modified Foley catheter used for obtaining such roentgenograms. Since these pictures were taken, two of our residents, Drs. Davis and Cian, have perfected a special type of catheter which permits filling of the urethra by obstructing the urethra at both the distal and proximal ends.

Treatment consists of excising the diverticulum with the necessary plastic repair of the urethra (Figs. 3 and 4). The results on the whole have been very gratifying, but there are occasional sequelae, such as the persistence of a long-standing bladder infection, urethral stricture, and urethral fistula. The stricture is usually not dense and is easily overcome by dilatation. The few urethral fistulas have usually been asymptomatic, only one of ours requiring repair.

The point which I would like to make regarding this condition is that it is a possible explanation for every case with persistent symptoms of "cystitis" and one should not fail to search for it.

Fig. 2.—Foley catheter with holes cut in to permit filling of the diverticulum. Catheter has also been tied off just distal to the balloon.

During the past decade or more, considerable progress has been made in the treatment of urinary incontinence in the female. It was in 1914 when Kelly first reported on 20 cases of stress incontinence of urine, treated by simple sphincter plication. In 16, the operation was successful. Kelly plicated only at the internal sphincter region. Since then, we have modified his original procedure in an attempt to utilize all of the circular muscle fibers throughout the length of the urethra by plicating the urethra throughout its full lengh (Fig. 5). Our results on the whole have been very good, especially when the incontinence is dependent upon a cystourethrocele, which is repaired at the same time. There is a small percentage of failures, however, when more extensive procedures need be utilized to make the patient continent. These are chiefly cases of incontinence in elderly women without cystourethrocele and cases with much scar tissue in the region of the sphincter from previous surgery.

There are two types of operative procedures that are carried out generally for these more difficult cases, the Goebell-Stoeckel type of fascial sling operation and the Marshall-Marchetti retropubic operation. I have personally performed the Goebell-Stoeckel type of operation in some modification more than

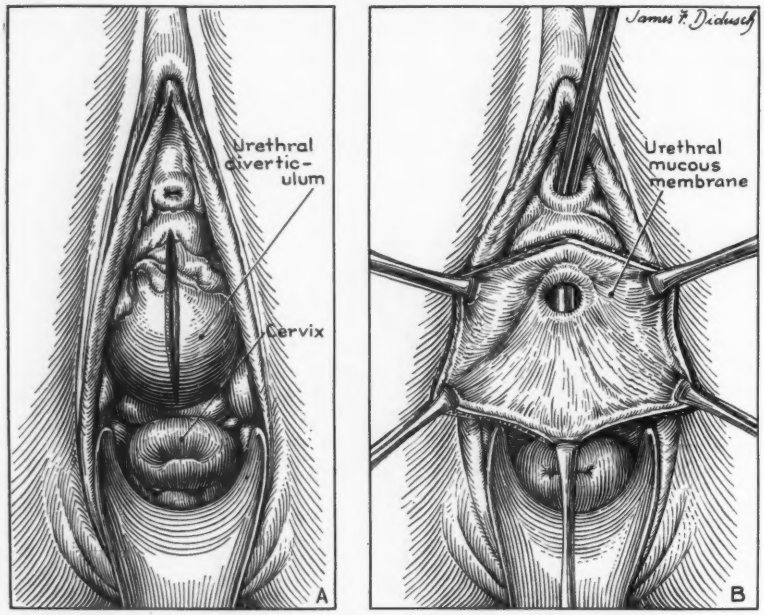

Fig. 3.—*A*, Bulging urethral diverticulum has been incised. *B*, The lining of the diverticulum visualized. With a glass catheter in the urethra the opening is visualized. (From Te Linde: Operative Gynecology, ed. 2, Philadelphia, 1953, J. B. Lippincott Company.)

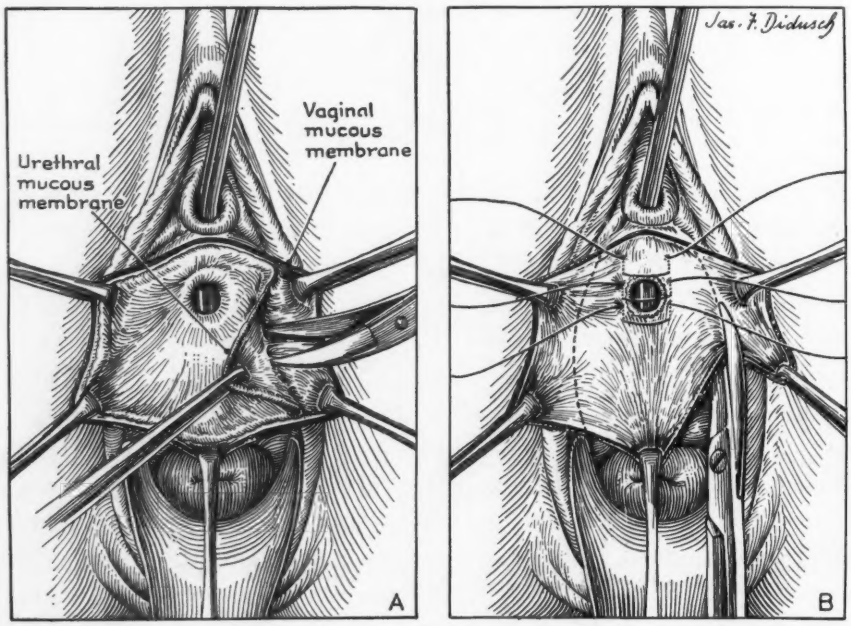

Fig. 4.—*A*, Mucosal lining of the sac is excised directly under vision, care being taken as the opening into the urethra is approached not to injure the urethra. *B*, The closure of the urethral defect is begun. (From Te Linde: Operative Gynecology, ed. 2, Philadelphia, 1953, J. B. Lippincott Company.)

fifty times with a few failures but, on the whole, very satisfactory results. Fig. 6 illustrates the general principle of the strap operation done by the Aldridge modification. I have done two of these operations under local anesthesia, and although the anesthesia left much to be desired, I was able to demonstrate the action of these straps very well. When the patient was requested to cough, it was possible to demonstrate the upward pull on the straps at the exact moment when the patient with stress incontinence spurts urine. My experience with the Marshall-Marchetti operation is much more limited, but Marchetti's results have been quite satisfactory (Fig. 7). Its advantage is doing the operation through one operative field. I cannot give you the exact indications for one of these operative procedures over the other, except to say that when plastic work is also necessary on the anterior vaginal wall.

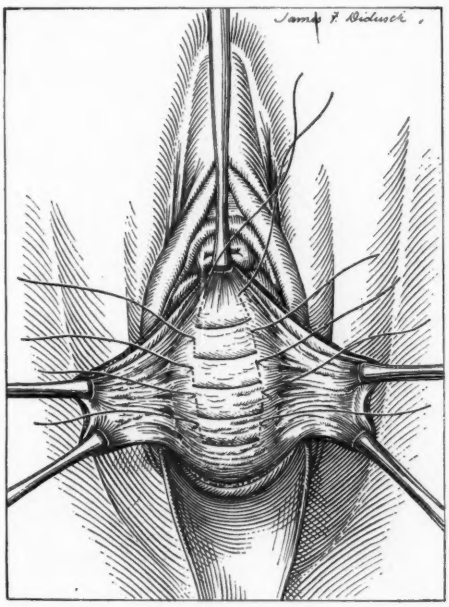

Fig. 5.—Plication of urethra throughout its full length with mattress sutures. (From Te Linde: Operative Gynecology, ed. 2, Philadelphia, 1953, J. B. Lippincott Company.)

I prefer the strap type of operation. I have had the experience of curing some cases with the sling type of operation after the Marshall-Marchetti operation had failed. On the other hand, I have recently cured a woman's severe incontinence by the Marchetti procedure, on whom I had failed with a previous sling operation. It is well for all pelvic surgeons to be familiar with these two procedures, for much can often be accomplished by either after simple plication has failed.

The intimate relationship between gynecology and urology is demonstrated by the various congenital anomalies which jointly affect both the generative and urinary apparatus from the embryological, anatomical, physiological, diagnostic, and therapeutic points of view.

Malfusion of the Müllerian ducts resulting in various degrees of double uterus and double vagina is associated with complete absence or malformation

of one kidney in about 20 per cent of the cases. Congenital absence of the vagina usually associated with the absence of the entire Müllerian duct system is likewise characterized by a high incidence of Wolffian duct anomalies.

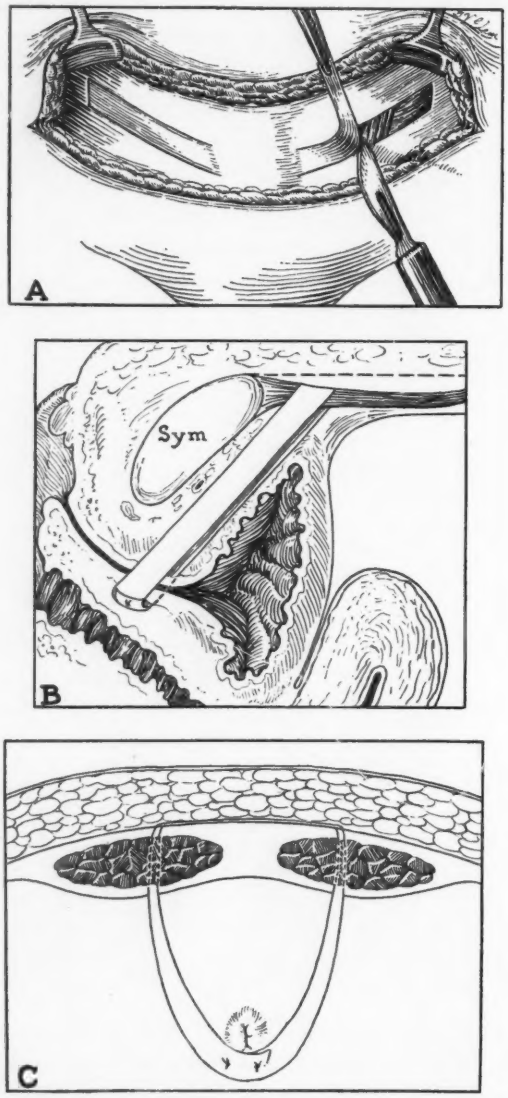

Fig. 6.—Illustrating the Aldridge modification of the Goebell-Stoeckel operation.
***A*, Transverse fascial straps are cut.**
***B*, Note the direct line of pull on the posterior urethra.**
***C*, Note how fascial straps perforate rectus muscles.**
(From Te Linde: Operative Gynecology, ed. 2, Philadelphia, 1953, J. B. Lippincott Company.)

Malformations of the urogenital sinus in females, so severe that sex identification by examination of the external genitals is misleading or impossible, require endoscopic diagnostic skills traditionally associated with the urologist but also demand procedures in an area familiar to the surgeon trained in vaginal plastic techniques (Fig. 8).

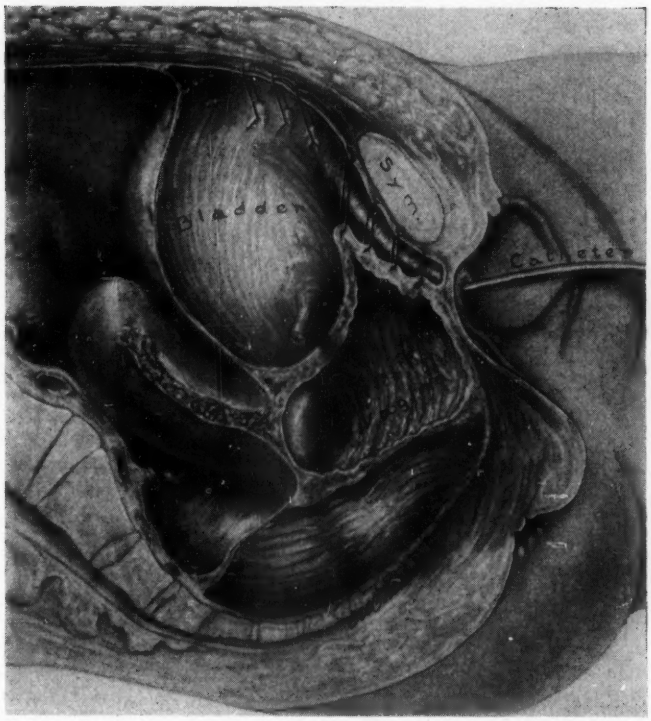

Fig. 7.—Marshall-Marchetti operation. (From Te Linde: Operative Gynecology, ed. 2, Philadelphia, 1953, J. B. Lippincott Company.)

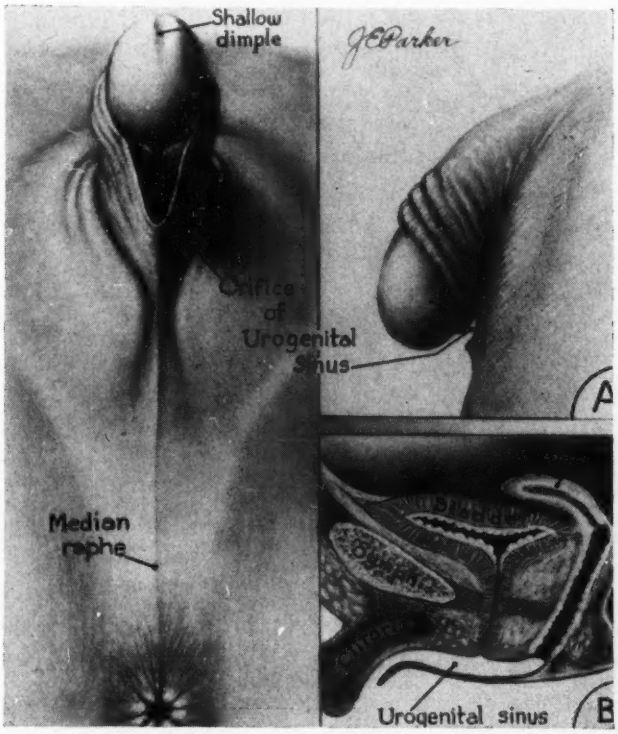

Fig. 8.—Showing usual configuration of genitals with adrenal hyperplasia.

The necessary endoscopic investigation preliminary to achieving the surgical goal of a functional vagina while retaining urinary continence and providing feminine-appearing genitals may be carried out at a single anesthetic seance if the embryological possibilities, the anatomical relationships, and the physiological purposes and requirements of the urological and reproductive systems are kept clearly in mind.

The relationship between gynecology and urology may be emphasized by mentioning the fact that both the generative and urological systems may be involved in three important diseases, carcinoma, gonorrhea, and tuberculosis. This fact is well known, but perhaps the relation between certain other common major gynecological conditions, such as large fibroids, ovarian tumors, pelvic inflammatory disease, and prolapse, and the urinary system is not as well recognized. Some work had been done on this subject by Kretschmar and Kanter and also by Brettauer and Rubin. Everett and Sturges found, on making urological studies of 100 women suffering from these conditions, that exactly 50 per cent of them had some degree of dilatation of the upper urinary tract. They were somewhat surprised to discover that 36 per cent of the women whom they studied showed some degree of hypertension, since the average age was only 37 years. The incidence of hypertension was 50 per cent in the patients with upper urinary tract dilatation and only 22 per cent in those without demonstrable upper tract dilatation. On comparing these figures with those from a control series, it seems warranted to conclude that arterial hypertension occurs with much greater frequency in women with pelvic masses and uterine prolapse than in women without these conditions.

The destructive effect of advanced cervical cancer on the urinary tract has long been recognized as evidenced by vesicovaginal fistulas and death from uremia. In 1939, Everett began a series of studies to determine earlier changes in the urinary tract due to cervical cancer and irradiation therapy. He first made a complete study of the urinary tract in 46 patients with cervical cancer before any treatment had been instituted to determine what, if any, prognostic value such as a urological study might have. Ureteral obstruction was found with none of the Stage I or Stage II cancers, but was found with 57 per cent of the Stage III cancers. None of these patients, in whom pretreatment ureteral obstruction was demonstrated, were cured by irradiation, but of the 12 patients whose cancer had been classified as Stage III but who did not show evidence of ureteral obstruction, 75 per cent survived. This suggests that the induration and fixation felt in the parametrial regions may have been due to inflammatory reaction rather than extension of the carcinoma. From these observations, it seems likely that the urological examination was more helpful in evaluating the prognosis than the bimanual palpation of the parametrial regions.

In Everett's urological studies on carcinoma patients *after* treatment, he confirmed the findings of many others regarding the bladder—primary erythema within twenty-four hours after treatment, secondary erythema appearing usually about four weeks after treatment, and the tertiary lesion occurring years later and consisting of endarteritis, sloughing, and a persistent

ulceration. He concerned himself more especially with a new concept, the possible effect of irradiation therapy on the upper urinary tract. Autopsy findings by Hunner and Everett, together with a case reported by Schmitz, seemed to indicate that irradiation per se is capable of causing ureteral obstruction with resultant hydronephrosis. Everett's studies showed that about 50 per cent of the irradiated patients who showed no dilatation before treatment, showed some degree of ureteral obstruction, but in only about 15 per cent were the lesions sufficiently severe to be of clinical importance. The more serious lesions predominated in the cases in which the follow-up had been longer, indicating the progressive sclerosing effect of irradiation and suggesting that urological investigations and treatment from time to time after irradiation are of value in preserving kidney function. The late irradiation ureteral strictures are extremely difficult to dilate, whereas, if attacked earlier, they yield more easily.

In 1949, Everett, Brack, and Farber made further studies on the effect of irradiation therapy upon the urinary tract. In 1940 our standard technique for irradiation of cervical carcinoma was changed from the method of a single dose over a short period of time, the technique upon which Everett's early study was based, to that of a divided dose of radium with a two-week interval, followed by a full dosage of x-ray. In Stages I and II, the radium is usually given first and the roentgen therapy started two weeks later. In the more advanced cases, the x-ray treatments are administered first, followed by the radium. In this second study, the authors showed that the incidence and severity of urological complications were greatly reduced by achieving the desired milligram hour dosage with smaller amounts of radium administered over a longer period of time. They also demonstrated the value of the early detection of recurrences by cystoscopic examination. Thus, by these studies upon the urinary tract, we have gained important knowledge regarding prognosis and therapy of this most important gynecological disease.

Since the Wertheim operation, with its many urological complications, is again in vogue in several clinics in the country, I wish to say a word about it, especially in relation to urinary tract complications. After carefully reviewing the results of those clinics in which the Wertheim operation is used extensively for Stage I cervical cancer and comparing them with our results with irradiation therapy, we have found no reason to alter our recent and present practice of treating Stage I, as well as Stages II, III, and IV, with irradiation. The surgical results in the hands of the *best* operators are no better than the results with irradiation, and the urinary complications, such as incontinence, uretero- and vesicovaginal fistulas, are much greater. In the hands of the *average* surgeon, the results with surgery are definitely poorer and the urological complications much greater. We reserve the Wertheim type of operation with pelvic lymphadenectomy for the cases of Stage I cervical cancer which prove to be resistant to irradiation. It is true that the danger of ureterovaginal fistula is increased by irradiation plus lymphadenectomy, but the operation is a calculated risk which we believe is justifiable when we are giving the patient her only chance of survival.

I should like to insert a word here in reference to preoperative ureteral catheterization in certain selected cases in which there is reason to believe that there may be greater than usual danger to the ureter. I refer to cases of cervical myoma, intraligamentary tumors, and large adherent ovarian tumors. Also, when the modified Wertheim operation for cervical carcinoma in situ with wide broad ligament excision without lymphadenectomy is done, we routinely catheterize the ureters before operation. With the true Wertheim type of radical hysterectomy with pelvic lymphadenectomy necessitating dissection of the ureters, it is not as essential, but when the woman is excessively obese, or if there is induration in the broad ligament region, ureteral catheterization may be advantageous. The knowledge of the position of the ureters, readily obtained by palpation at all times during the operation, is of great comfort to the operator and may save much operating time. I have never seen any evidence that the presence of a catheter in the ureter was a predisposing factor in ureteral fistula formation. On the other hand, I am certain that many a ureteral injury has been avoided on our service by preoperative ureteral catheterization.

Since I have admitted that we are responsible for some vaginal urinary fistulas, perhaps I should say something about our method of handling them when they occur postoperatively. Filling the bladder with methylene blue easily establishes whether the fistula is vesical or ureteral. If it proves to be a bladder fistula, the patient should be advised of her condition and sent home for six months and asked to take weak vinegar douches to get her vaginal tissues in good condition. Then we firmly believe that the operation described by Latzko for its repair is the operation of choice (Fig. 9). I can honestly say that I have not failed to cure a posthysterectomy vesicovaginal fistula since using this technique during the past ten or more years. The shortening of the vagina is usually negligible.

If the urinary vaginal fistula proves to be ureteral, cystoscopic examination is done shortly after the appearance of the fistula, and an attempt is made to catheterize both ureters. Very rarely will it be possible to pass a catheter beyond the site of injury in the ureter. If it is accomplished, the catheter should be left in for 10 or more days with the hope of healing. A phthalein test should be done with a catheter up the uninjured ureter to establish the function of the kidney on the uninjured side. The patient is then followed with intravenous urography at intervals of ten days. We do not believe that an attempt should be made at repair of the injured ureter in less than six weeks, and a longer delay is desirable. If intravenous urography indicates the development of considerable hydronephrosis or if there is fever due to kidney infection before the lapse of six weeks, pyelostomy or nephrostomy should be done to save the kidney function while several weeks are allowed for the pelvic tissues to get into condition for the reparative operation. The exact reparative procedure depends upon the location of the injury. In general, reimplantation of the ureter into the bladder is easier and more certain of success than ureteroureteral anastomosis.

The implications of urology in relation to modern ultraradical surgery are great. First, may I state that our attitude toward the indications for such surgery is a very conservative one, but we do believe it has a very limited place in the treatment of irradiation-resistant cervical cancer. The diversion of the urinary stream has been and is one of the major problems in such surgery.

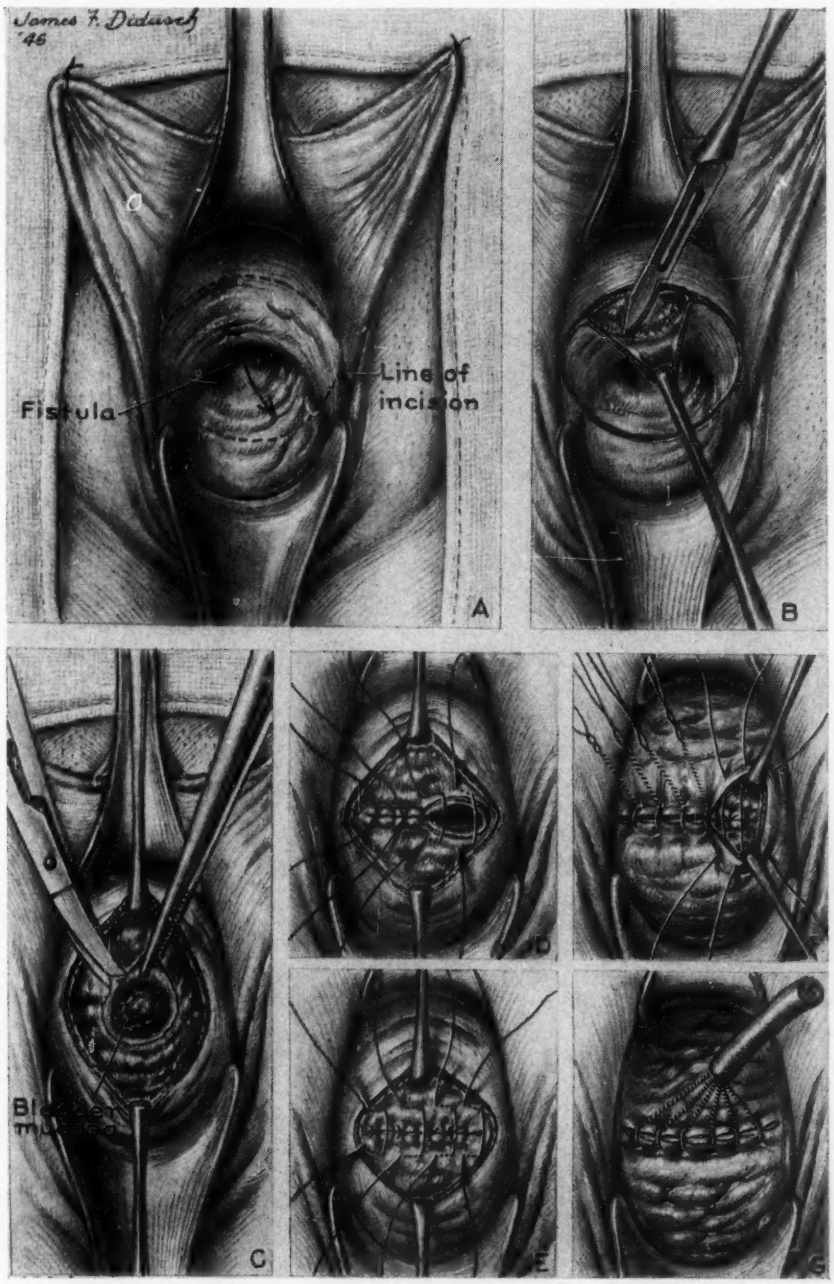

Fig. 9.—Latzko operation for vesicovaginal fistula following total hysterectomy. Notice that the anterior and posterior vaginal walls are utilized to close the fistula. (From Te Linde: Operative Gynecology, ed. 2, Philadelphia, 1953, J. B. Lippincott Company.)

Fig. 12.

Fig. 11.

Fig. 10.

Fig. 10.—Intravenous pyelograms before ureteral stricture.
Fig. 11.—Intravenous pyelogram showing hydronephrosis after ureteral stenosis.
Fig. 12.—Intravenous pyelogram two weeks after implantation into loop of ileum.

Also, in connection with benign conditions such as incurable vesicovaginal fistulas, exstrophy of the bladder, and congenital absence of vesical sphincter, we have found it useful to divert the urinary stream. The experience of our clinic in such cases extends over many years. It has been amply demonstrated that the implantation of the ureters into the sigmoid often shortens the patient's life. There are some notable exceptions to this rule. For example, we have one patient in our clinic, living and well, whose ureters Hunner implanted into the rectum through the vagina 21 years ago for an incurable vesicovaginal fistula. Nevertheless, in the majority of cases, hydronephrosis, hyperchloremic acidosis, and potassium deficiency result sooner or later, and the patients die in uremia. Recent work in the urological department of our hospital, done upon the kidneys of patients who died after ureterosigmoid anastomosis, has shown the kidneys to have a histological picture typical of potassium deficiency. The urologists have also found that hyperchloremic acidosis and potassium deficiency do not develop when the ureters are implanted into an isolated loop of ileum with free drainage onto the abdomen. They have seen such a contrast between the ileal loop patients and the sigmoid implantation patients that they have removed several previously implanted ureters from the sigmoid and reimplanted them in isolated ileal loops as described by Bricker. Their work is confirmatory of Bricker's, who had no patients develop hyperchloremic acidosis in 106 cases; however, the procedure is a fairly formidable surgical undertaking. We have recently had one death and Bricker reports 15 deaths in his 106 cases, 5 of which were definitely attributable to the operative procedure.

Encouraging as our experiences have been with the ileal loop, we are not yet willing to scrap the ureterosigmoidostomy. The continence of the urine held in the rectum and colon is a real advantage over the incontinence of the ileal loop technique. On the other hand, the percentage of patients with persistently normal pyelograms and freedom of attacks of upper tract infection is much greater with the freely draining ileal loop than in the ureterosigmoid cases. In making ureteroileal anastomoses we have used the mucosa-to-mucosa technique of Cordonnier which appears to be more satisfactory than the less meticulous techniques.

Two concrete examples will illustrate our experiences.

Mrs. McC. was a woman of 30 who had had a kidney removed for tuberculosis. Some years later, she presented herself at our clinic with absence of the vesicovaginal septum. She stated that complete incontinence had developed suddenly several years after her nephrectomy and several months after the birth of her only child. The exact cause of her large fistula was never determined. Several unsuccessful attempts at repair were made. Several months after the last attempt she developed complete anuria due to obstruction of the lower end of the ureter at the bladder wall, apparently due to scarring. Fig. 10 shows the intravenous urogram before this occurred and Fig. 11 demonstrates the hydronephrosis which developed after the ureteral occlusion. The hydronephrosis became infected and a nephrostomy was done for temporary relief and to permit improvement in her general condition. When this had improved sufficiently, a loop of ileum was isolated and the sole ureter implanted into the loop. Fig. 12 shows the normal intravenous urogram taken two weeks after the implantation. The blood chemistry values are now

Fig. 13. Fig. 14. Fig. 15.

Fig. 13.—Normal intravenous pyelograms before ureterosigmoid anastomosis.
Fig. 14.—Intravenous pyelograms showing hydronephrosis at nine months after ureterosigmoid anastomosis.
Fig. 15.—Intravenous pyelograms which show return to normal two weeks after implantation into ileal loop.
(From Te Linde: Operative Gynecology, ed. 2, Philadelphia, 1953, J. B. Lippincott Company.)

normal, and the patient, who was emaciated, has returned to a normal weight. During the period of time when she had to contend with the fistula, she became morose and alcoholic. The bag which she wears for the collection of the urine seems to her a small price to pay for relief of her incontinence and complete physical and mental rehabilitation.

C. L. had had one kidney removed for renal calculi. She had had urinary difficulties for years due to congenital folds in the urethra. These had been repeatedly resected and she ultimately developed complete urinary retention with a large atonic bladder. After years of self-catheterization and many episodes of acute retention due to her inability to pass the catheter, it was decided that some type of definitive therapy should be undertaken. Fig. 13 shows her normal pyelogram before ureterosigmoid anastomosis on June 3, 1955. Following this implantation she developed hyperchloremic acidosis, pain in the flank, and one attack of acute pyelitis. The intravenous urograms taken 9 months after the operation showed the development of marked hydroureter and hydronephrosis (Fig. 14). Blood chemical studies showed hyperchloremic acidosis. Because of the deteriorating urological condition, it was decided to implant the ureter into an isolated loop of ileum. Intravenous urograms, taken two weeks after the operation, showed a return to normal (Fig. 15) and have remained so. Her blood chemistry values have remained normal.

These are but two examples of ileal loop ureteral transplantation, but the results to date are encouraging. Nevertheless, we would be the first to admit that the last word has not been said on the important subject of diversion of the urinary stream, and much experimental and clinical work remains to be done.

I hope I have given you sufficient evidence in this lecture to illustrate the close relationship between gynecology and obstetrics and urology. But urology is only one of the various facets of our specialty not yet sufficiently developed, but closely related to gynecological surgery. As I conceive of modern gynecology, it is a broad specialty and embraces much more than operative work. In addition to training in female urology, the gynecologist of the future should be trained in gynecological and obstetrical pathology. This is the very foundation upon which good gynecology is practiced. He should have a knowledge of the fundamentals of endocrinology in its relation to obstetrics and gynecology, and finally, but by no means least important, he should have an appreciation of psychiatry as applied to our specialty, a phase which to date has been unfortunately greatly neglected. It is only by developing our specialty along these broad lines that we can defend ourselves against the general surgeons who perform hysterectomy but fail to appreciate that the technical ability to perform this operation does not justify their care of the women of our country.

A CLINICAL EVALUATION OF URETHROVESICAL LYSIS FOR THE CURE OF URINARY STRESS INCONTINENCE IN THE FEMALE

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DURING the past twenty years, many ingenious procedures have been devised to alleviate the distressing condition known as urinary stress incontinence in the female. These have ranged from the simple vaginal repair to the more complicated urethral sling and suspension operations, all of which have their proponents.

Since the majority of women with urinary stress incontinence have an associated cystocele, an adequate repair of this relaxation usually results in a cure of the incontinence. Therefore this approach should be carried out initially in the majority of cases. In some women, however, in whom one or more vaginal repairs have not cured the incontinence, or in whom the incontinence has appeared following the repair, other measures may not infrequently be required. In nulliparous women who show no evidence of vaginal relaxation, but who have stress incontinence, procedures other than a vaginal repair may be warranted initially.

Following the most lucid report by Mulvany[1] in 1951, in which he described a new approach in the treatment of certain selected cases of stress incontinence, we became interested and intrigued by the simplicity of the procedure and by the good results that had been obtained. It was decided to carry out Mulvany's method of urethrovesical lysis in all appropriate cases and to scrutinize the results from an impartial viewpoint. Since cases that fit into a careful selection category are not plentiful, we have been able to collect 14 and adequately follow 13 cases during the past four years (Table I).

Investigation of the Case

In all cases of urinary stress incontinence, each patient must be carefully investigated to rule out any unsuspected cause of the incontinence. This includes a detailed history, complete physical examination, and any laboratory procedures which will prove of value in assessing the case.

An attempt should be made to demonstrate the stress incontinence. This is most readily accomplished by filling the bladder and then having the patient walk and strain down. When this is demonstrated, one should carry out

Marshall's test in which temporary support is offered at the urethrovesical junction. If the incontinence is temporarily cured by this procedure, then the patient should benefit from the lysis procedure.

An interesting investigative procedure that should be done both pre- and postoperatively in these stubborn incontinence cases is the radiological study of the bladder by means of cystograms. Prior to Jeffcoate's[2] publication a few years ago, it was common to take only anterior views of the bladder. In some cases these views may show changes postoperatively when they are compared with the preoperative film. Of more interest, however, are the lateral views of the bladder. These may be taken when the patient is at rest, during straining, and when voiding.

TABLE I. REVIEW OF 14 CASES TREATED BY THE OPERATION OF URETHROVESICAL LYSIS

PATIENT	AGE	PARITY	PREVIOUS REPAIRS	OTHER PELVIC PROCEDURES	ASSOCIATED CONDITIONS	TIME SINCE LYSIS	RESULT
M. M.	39	ii	1	Previous hysterectomy	—	3 years	Excellent
H. L.	53	i	0	—	—	3 years	Excellent
M. P.	32	ii	0	Previous hysterectomy	—	3 years	Excellent
M. P.	35	i	0	Salpingo-oophorectomy	Bronchitis	3 years	Not improved
L. H.	35	ii	1	Urethral sling	—	3 years	Excellent
E. L.	73	i	1		—	3 years	Excellent
S. S.	41	iii	0	Hysterectomy at same time	—	3 years	Excellent
E. T.	65	i	1	Hysterectomy	—	3 years	Excellent
P. M.	50	i	1	—	—	3 years	Moderately good
F. T.	47	v	1	—	—	3 years	Excellent
P. M.	48	i	1	—	—	6 months	Moderately good
J. S.	66	ii	0	Previous hysterectomy	—	5 months	Not improved
M. G.	42	i	1	—	—	3 years	Moderately good
J. F.	39	ii	1	—	—	3 years	Not improved (not followed)

Procedure

Mulvany's initial reasoning to justify his operation of urethrovesical lysis was based on the fact that the so-called internal sphincter is unable to function properly because of the presence of distorting adhesions, resulting from previous operation, childbirth, or degeneration. This author maintained that if the bladder neck were freed of any interfering scar tissue it would in all probability function in a normal fashion.

To accomplish this, the approach which may be chosen to free these distorting adhesions is by means of extraperitoneal dissection into the space of Retzius on either side. A transverse or longitudinal subumbilical incision is made. The rectus muscles are separated and the bladder neck and urethra are readily identified. Previous insertion of a Foley catheter makes the dissection somewhat easier.

In the majority of cases the urethra will be found to be in close proximity to the symphysis. By means of blunt dissection with the index finger, the urethra is separated anteriorly and laterally on both sides. The anterior and

lateral pubovesical ligaments may be cut as well, to provide a freer relaxation of the sphincter area. The urethra and bladder neck are then found to be quite movable anteriorly and laterally. No attempt is made to free the urethra posteriorly where it is intimate with the vagina.

Very little bleeding is encountered in the space of Retzius as a rule and the incision is closed in layers. Should troublesome oozing be met with, a drain may be inserted and removed in a few days.

The procedure takes about 15 or 20 minutes, and since the peritoneal cavity is not entered, the reaction of the patient is slight. The catheter is removed the following day and the patient allowed up and around.

Results

In this series, 14 patients were subjected to the urethrovesical lysis procedure for the treatment of urinary stress incontinence. One case was lost as far as follow-up was concerned, thus leaving 13 patients who were followed. Of these 13, 8 had had one previous vaginal repair; 1 had had a previous sling procedure which had followed a previous vaginal attempt; 5 operations were done as initial attempts, 2 accompanying pelvic surgery because of other pathological conditions and 3 as the initial approach in nulliparous women with no demonstrable cystocele.

The follow-up period in the cases studied ranges from 3 years to 5 months. Of the 13 cases in which this procedure was done and followed, 8 have an excellent result, that is, they have no stress incontinence at any time; 3 have a moderately good result, e.g., incontinent on rare occasions; 2 were not helped by the procedure.

It can be seen from the results that 11 of the 13 patients followed were helped by the procedure; 2 patients received no benefit. If the unfollowed patient is classified as a failure, then 3 patients out of 14 were not helped by the procedure.

Comment

A method of relieving the distressing condition of urinary stress incontinence in the female has been reviewed. This series followed the introduction of the approach by Mulvany in 1951 and reviews the results in 14 cases. The principle of the operation is based on allowance of the internal sphincter to function properly after the freeing of the distorting adhesions which interfere with it. The underlying principles of this procedure are basically similar to those advanced by Kennedy[3, 4] who maintained that it was most important to free the base of the bladder widely laterally before plicating the supporting fascia in cases of incontinence.

Lennon[5] has undertaken to carry out Mulvany's principles by using a slightly different approach. Access is gained to the base of the bladder and proximal urethra by dissection carried out inwardly between the clitoris and urethra. In this way somewhat the same result may be obtained by means of the abdominal approach.

It is interesting to note that the procedure described by Mulvany is actually the same as the initial steps of the Marshall-Marchetti[6] operation. No suspensory sutures are used in the lysis procedure, however. The idea has been advanced by Chalmers[7] and Stabler[8] that Mulvany's lysis operation works by producing adhesions which anchor the urethra and bladder neck to the back of the pubis again, and have the effect in the end, of a vesicourethral suspension. However, relief from incontinence is seen immediately following the lysis operation, long

before adhesions would have time to form any type of suspension. This leads one to believe that allowance of the sphincterlike mechanism to work properly by freeing the adhesions is of more importance than any suspensory support.

The radiological study of the urethra and bladder both pre- and postoperatively in these cases is quite interesting. The importance of the posterior urethrovesical angle stressed by Jeffcoate was not demonstrated in our series. Incontinence may be present despite a good angle and continence may be seen postoperatively following this procedure, despite the absence of the posterior urethrovesical angle at rest.

Elongation of the urethra postoperatively as seen radiologically was a more constant finding than change in the posterior urethrovesical angle.

It is quite obvious that the follow-up period is not as long as would be desirable. It allows us to think, however, that this procedure does warrant a place in the armamentarium of those confronted by obstinate cases of urinary stress incontinence.

Summary

A review of 14 cases of urinary stress incontinence treated by means of the urethrovesical lysis procedure described by Mulvany has been carried out. Thirteen of these cases were adequately followed. One was lost in the follow-up and is classified as a failure. Many of these women had undergone previous vaginal surgery in an attempt to eliminate their incontinence. The lysis operation, which is very easy to perform, gave excellent results in 8 cases, and improvement in 3 cases; 2 received no benefit from the operation, and on one there is no late information.

It seems justified to conclude that this procedure is of value in the treatment of stress incontinence in the female in properly selected cases.

We should like to express our appreciation to members of the Gynaecological Staff at St. Michael's for their permission to include some of the cases included in this series.

References

1. Mulvany, John H.: J. Obst. & Gynaec. Brit. Emp. **58**: 449, 1951.
2. Jeffcoate, T. N. A., and Roberts, Henry: AM. J. OBST. & GYNEC. **64**: 721, 1952.
3. Kennedy, W. T.: AM. J. OBST. & GYNEC. **34**: 576, 1937.
4. Kennedy, W. T.: AM. J. OBST. & GYNEC. **52**: 206, 1946.
5. Lennon, G.: J. Obst. & Gynaec. Brit. Emp. **59**: 717, 1952.
6. Marshall, V. F., Marchetti, A. A., and Krantz, K. E.: Surg., Gynec. & Obst. **88**: 509, 1949.
7. Chalmers, J. S.: J. Obst. & Gynaec. Brit. Emp. **59**: 77, 1952.
8. Stabler, F.: J. Obst. & Gynaec. Brit. Emp. **59**: 708, 1952.

Obstetrics

MASSIVE HYPERTROPHY OF THE BREASTS AND AXILLARY BREASTS IN SUCCESSIVE PREGNANCIES*

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MASSIVE mammary hypertrophy is an uncommon condition. While the majority of cases have their onset during adolescence, a similar condition may arise during pregnancy. Geschickter[1] collected 27 cases, of which only 2 showed enlargement associated with pregnancy. Burslem and Dewhurst[2] reported 2 cases of massive hypertrophy of the breasts that occurred in early pregnancy. In my patient, massive hypertrophy of the breasts occurred early in her first pregnancy; axillary breast hypertrophy occurred in a succeeding pregnancy.

It is likely that the mammary response to the hormone influence of gestation is excessive, or that there is an overproduction of hormones affecting breast growth. The growth of the breast is said to consist of an extension of ducts with marked increase in the periductal interlobar connective tissue. There is a moderate lymphocytic infiltration. In the later stages hyalinized connective tissue is found. Localized fibroadenomas, as in this case, may occur.

Case Report

H. C., a 31-year-old Negro woman, para 0, gravida ii, whose last menstrual period was June 17, 1951, was first seen on Oct. 1, 1951, because of "excessive size of both breasts, dyspnea on exertion, and orthopnea." The "swelling of the breasts" began on July 13, 1951, and they had continued to increase in size until it was necessary to support each breast in a separate large bath towel. The patient stated that prior to pregnancy she wore a "size 40" brassière. In 1949 she was advised to have a plastic repair of the breasts because of the size.

The blood pressure was 108/60, her weight was 200 pounds, and her height was 5 feet, 4 inches. The heart and lungs were normal. She was 15 weeks pregnant, with normal pelvic measurements.

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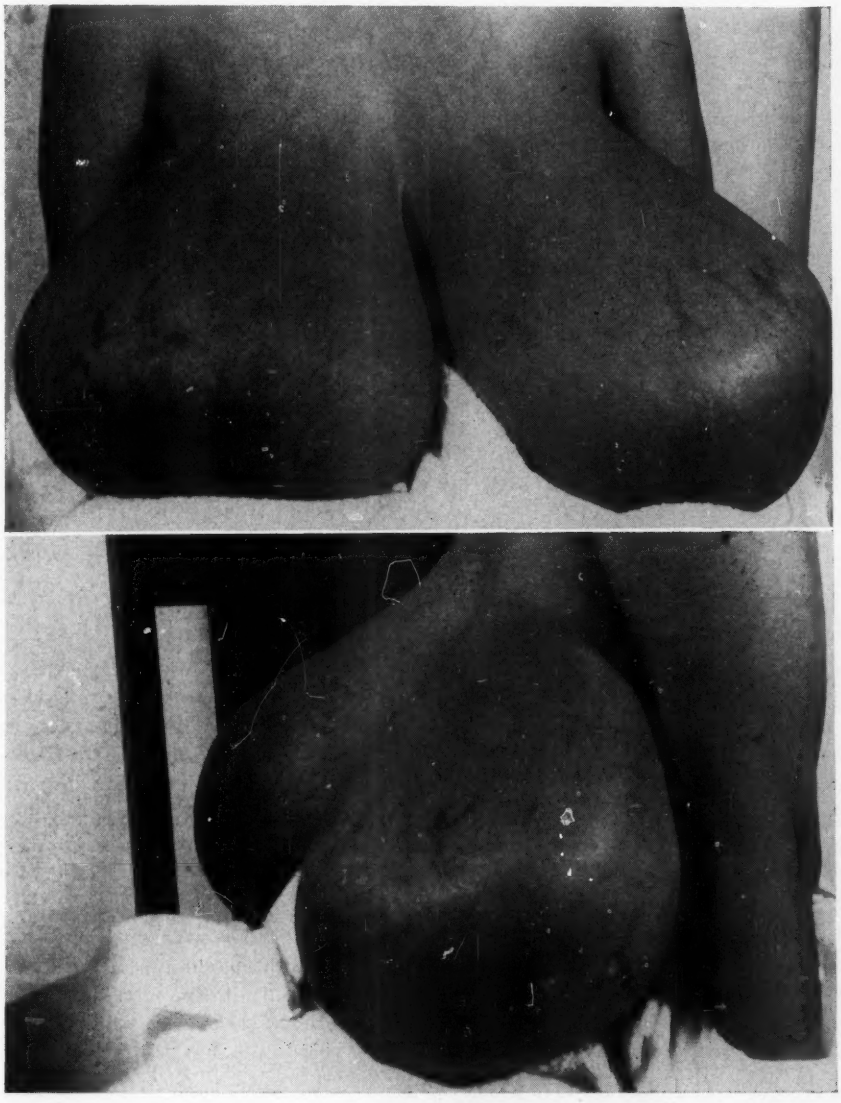
The right breast measured 35 by 25 cm., overlying the suprasternal notch above and the right anterior axillary line laterally. The skin was markedly hyperemic and edematous, and many large, tortuous and dilated veins could be seen over the surface. Small lesions were seen at various levels over the mammary glands, especially in the dependent portion (Fig. 1, *A* and *B*).

The left breast measured 30 by 22 cm. and was of similar description.

Because of the symptoms and the tremendous size and marked ulceration of both breasts, bilateral simple mastectomies were considered the procedure of choice.

A.



B.

Fig. 1.—*A*, Anterior view of breasts; both weighed 12.57 kilograms. *B*, Lateral view.

The patient was admitted to Provident Hospital on Oct. 7, 1951. The urine was normal; the hemoglobin was 9.6 grams per cent; the red blood count was 3.7 million; the white blood count was 6,200 with a normal differential; the blood was type O, Rh positive. A transfusion of 500 c.c. of blood was given to the patient on Oct. 8, 1951.

On Oct. 10, 1951, through a modified Stewart incision, bilateral simple mastectomies were performed. The patient received 2,000 c.c. of whole blood during the operation. The postoperative course was uneventful and she was discharged on the eighth postoperative day in excellent condition. Her weight, 200 pounds before operation, was now 160 pounds.

The pathologist's report showed fibroadenoma of mammary gland tissue, hypertrophy and hyperplasia of the mammary gland with lactogenic effect.

Gross Description.—(Left and right breasts.) The left mammary gland, now flattened out, was 44 by 30 by 6.5 cm. and weighed 6,290 grams. The tan-brown areola was 11.5 cm. in diameter and the nipple was 1 by 0.5 cm. On the surfaces made by cutting, the tissues were gray and fibrillar, intermingled with fat. At some levels there were tan-brown nodules ranging to 3.5 cm. in diameter. The right mammary gland was approximately 42 by 30 by 6.5 cm. and weighed 6,280 grams. The tan-brown areola was 14 cm. in diameter and the nipple was 1 by 0.2 cm. In one region there was an ulceration 5 cm. in diameter. On the surfaces made by cutting frontally, the tissues were tough and fibrillar and at some levels there were tan-brown nodules ranging to 3.5 cm. in diameter.

Fig. 2.—Axillary breasts; both weighed 0.48 kilograms.

Microscopic Description.—These mammary gland tissues from many levels had thick connective tissue septa supporting many proliferating ducts and groups of acini. At some levels there were secretion vacuoles in the cells of the acini. At one level a dilated duct contained a fibroadenoma of loosely constructed connective cells with a proliferating epithelial lining. There was no unusual change of the epidermis in the skin on these sections. In the corium there was much hyalinization of the connective-tissue cells.

The remainder of the prenatal course was uneventful. On March 25, 1952, the patient was delivered of a full-term male infant who weighed 6 pounds, 2 ounces. The puerperium was complicated by mild enlargement of both axillary breasts. This was controlled by stilbestrol therapy.

On Nov. 11, 1952, the patient had a spontaneous abortion at 2 months. On April 6, 1953, the patient was again seen when 16 weeks pregnant with bilateral axillary breasts. In spite of testosterone therapy the breasts increased so markedly in size in the next two months that the patient was most uncomfortable and unable to lower her arms at her sides. The breasts were edematous and had begun to ulcerate, especially the left breast. She was advised to have both axillary breasts removed (Fig. 2).

On June 26, 1953, she was admitted to Provident Hospital with a history of having bled profusely from the ulcerated lesion in the left axillary breast. On admission the blood pressure was 96/50, pulse 112, hemoglobin 6 Gm., and the hematocrit 22 volumes per cent. Because of the anemia, the patient was given 1,000 c.c. of blood. On June 29, 1953, both axillary breasts were removed. In the postoperative period she received an additional 1,000 c.c. of blood and was discharged in good condition on the eighth postoperative day.

The pathologist's report showed marked pregnancy hypertrophy of aberrant axillary mammary gland tissues.

Gross Description.—The left axillary tumor was composed of lobulated tissue measuring 13 by 14 by 7 cm. and weighed 250 grams. It was covered with tan-brown skin measuring 15 by 11 cm. In one region there was a defect 3 cm. in diameter. On the surfaces made by cutting, the tissues were gray yellow and nodular similar to those of pregnancy hypertrophy. The right axillary tumor mass measured 11 by 10 by 6 cm. and weighed 225 grams. It was covered with tan-brown skin along one edge, measuring 13 by 12 cm. The description of the cut surface was similar to that of the tumor on the left.

Microscopic Description.—The histological preparations showed mammary-gland tissues with a fibrous stroma divided into lobules by fibrillar septa. In the lobules were many acini ranging from small to medium to large, lined by cuboidal epithelium. In the lumina of the acini there were eosinophilic precipitates. At some levels there were also many markedly dilated ducts. In the lumina of these ducts there were also eosinophilic precipitates.

The patient was delivered of a full-term female infant weighing 5 pounds, 14 ounces, on Sept. 16. 1953.

Subsequent Pregnancies.—On Aug. 24, 1954, this patient had a spontaneous abortion at 3 months.

On Dec. 18, 1955, she was delivered of a full-term female infant uneventfully. Neither pregnancy was complicated by the appearance of aberrant breast tissue.

Comment

It would have been ideal to attempt a plastic operation, removing the abnormal breast tissue and transplanting the nipple and areola. Here, however, we had rapidly growing breasts. There was no reason to suppose that these breasts would suddenly stop growing or that by removing a portion of them the rest would not grow. Geschickter and Wakeley[3] both stated that tremendous enlargement of the breasts with marked edema and atrophy of the nipple should influence the surgeon in favor of amputation rather than plastic surgery. Because of the excessive size of the breasts and axillary breasts in our case, simple removal was done.

Summary

1. A case is presented of massive hypertrophy of the breasts and axillary breasts in pregnancy.

2. Amputations of the breasts and axillary breasts were performed.

References

1. Geschickter, C. F.: The Diseases of the Breast, Philadelphia, 1943, J. B. Lippincott Company, pp. 116, 117.
2. Burslem, R. W., and Dewhurst, C. J.: J. Obst. & Gynaec. Brit. Emp. **59**: 380, 1952.
3. Wakeley, C. P. G.: Practitioner **132**: 608, 1934.

PUERPERAL BREAST ABSCESS*

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THE occurrence of puerperal breast infection has been reported at times, when seemingly there was a sudden outbreak or concentrated increase in the number of cases. Many authors, including Sherman[1] recently, Colbeck[2] in 1949, Knott and Blaikley[3] and Hobbs[4] in 1944, approached the subject from this aspect. The latter three made comparable statements that it was the impression of many obstetricians that outbreaks of breast abscess had become more frequent in recent years. That was in 1944, but despite the advent and liberal use of many antibiotics, the gravity of the situation has not lessened; if anything, it has become more serious. In a 10-year study of this problem we have found that although there are minor fluctuations when the incidence is higher than usual, there has been a relatively steady maintenance of this disease, except for the past 2 years when a marked increase has been noted.

In County Hospital practice, the type of patient, with her attendant economic status and social environment, has not altered; therefore, other factors must be evaluated. Contamination by hospital personnel has been regarded as a potent source of infection. The development of new or mutant strains of bacteria to which the patient has not acquired natural resistance, which are not sensitive to antibiotics, or are not controlled by modern aseptic techniques, has been demonstrated by numerous investigators. It is probably within this realm that the solution to the problem lies.

On examining Fig. 1 and comparing the ends of the scale, years 1945 and 1955, it is seen that although the deliveries have increased approximately three and one-half times, the number of abscesses has increased approximately eight and one-half times. In view of the shortage in hospital beds and space, one might interpret this to indicate that overcrowding and less efficient management as a consequence would in part account for the increase in infection. At the Philadelphia General Hospital[1] the annual delivery rate of approximately 4,000 per annum has not materially changed since 1950, yet they have experienced an upward surge in the number of breast abscesses, approximately three and one-half times as many occurring in 1955 as in 1950. In our series, hospital contamination does not seem to be the main or only source of infection, as suggested by other authors. In comparison with the Philadelphia General Hospital, except for the year 1955, our annual incidence of puerperal abscess is decidedly lower.

*Presented at a meeting of the Chicago Gynecological Society, Jan. 18, 1957.

Until 1954, there were small numbers of cases noted which were relatively evenly dispersed throughout the various months. Since then, when greater numbers of cases have been encountered, June, July, August, September, and October seem to be the peak months of the year, particularly in 1955. The appearance of cases has been more or less continuous, and periodic outbursts as reported by other authors[2, 5-7] did not occur in our series. Of late, there seems to be no particular month when the disease is not present in significant numbers.

Material

This study is based on 147 cases of breast abscess at the Cook County Hospital from June 1, 1955, through Dec. 31, 1955, in which bacteriologic cultures, methods of treatment, and follow-up are described and discussed. Control cultures were taken from the nipple and areola of patients admitted to the labor rooms and were repeated on the same patients on the day of discharge, in order to determine whether pathogenic bacteria normally inhabit the breast or if they are acquired possibly by hospital contact.

There were a total of 159 admissions, representing 12 readmissions for further therapy. Fifty-seven, 38 per cent, were primiparas. Breast manipulation occurred as follows: 111 nursed, 17 nursed and also utilized a breast pump, 16 only pumped the breasts, and 3 patients denied either procedure.

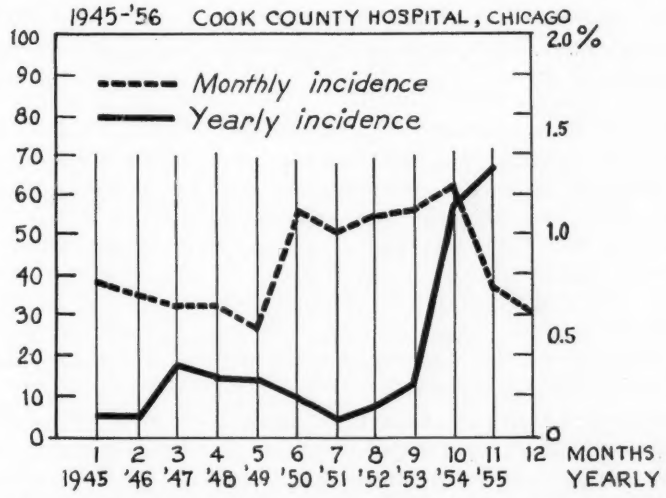

Fig. 1.—Per cent of total deliveries resulting in breast abscess on a monthly and yearly basis.

Symptoms and Lesions

In the majority of cases, 104, or 70.7 per cent, the onset of symptoms occurred between the eleventh and thirtieth days. In 30 cases the onset was prior to the eleventh day, in 7 cases between the thirtieth and fortieth days, and in 4 cases beyond 40 days. The shortest period was 2 days and the longest, 123 days.

The duration of symptoms prior to admission probably constitutes an important factor in the extent of the lesion in individual cases. In the majority, involvement included at least a quarter segment of the breast, both glandular and connective tissue, while in more severe cases practically the whole breast

was affected, being literally converted into a bag of pus. Lesser degrees of involvement, small localized glandular pockets or subareolar abscesses, were infrequent. Retromammary localization was not commonly found.

The average duration of symptoms prior to admission was 7.7 days, the earliest being one day in 2 cases, and the latest 21 days in 7 cases. The most common complaint was a painful lump or swollen breast. Cracked nipples were reported infrequently (8 cases) as antecedent to or associated with the infection. Spontaneous rupture occurred in 10 cases before admission. In 20 cases there was bilateral involvement. Other associated symptoms, such as chills, fever, or night sweats, were varyingly reported. Three patients mentioned concomitant infections elsewhere; one had bronchitis, one, postpartum endometritis for 8 days, and one, a swollen right wisdom tooth. Five patients had treatment prior to admission, consisting of cold packs and penicillin shots, which proved to be inadequate.

Etiology

The sources of pathogenic bacteria causing breast abscesses are manifold. No one source can be incriminated exclusively. On investigation, several authors have found a relatively high proportion of normal healthy adults and children who are carriers of coagulase-positive staphylococci. Martin and Whitehead[8] noted a total carrier rate of 62 per cent (nose, throat, saliva, and skin). Williams[9] obtained essentially similar results. Mouth washings of school children revealed 55.7 per cent, as determined by Matthews, Atkinson, Saunsbury, and Clegg.[10]

Duncan and Walker[11] have shown that the milk of a high proportion of nursing mothers, 92.7 per cent, becomes infected with *Staphylococcus aureus* during the first 10 days of lactation, and that this infection probably originates from the nasopharynx of the infant. Torrey and Reese[12] found 88 per cent of a group of newborn infants to be harboring *Staphylococcus aureus* at a time when there was no unusual incidence of staphylococcal infection. Martyn[13] examined cultures from the nasopharynx of 130 newborn babies and found a carrier rate of 50 per cent coagulase-positive staphylococci, of which 55 per cent were penicillin resistant, but only 3.7 per cent streptomycin resistant, at a time when the incidence of breast abscess in the hospital was approximately 10 per cent. Colbeck[2] found that discharge nose and throat swabs of 74 women revealed the pathogenic strain in only 2 cases. He concluded that the infant's nose and throat were the important reservoirs of infection, from which it was passed on to the mother's breasts.

Maternity and nursery personnel have been proved to be staphylococcus carriers and permanent sources of infection; 50 to 75 per cent among the staffs of four Winnipeg hospitals[2] and 31.7 per cent of the personnel in Pyle's[5] Maternity Department were discovered to be staphylococcus carriers.

It seems evident from the widely varying sources that, regardless of the patient's environment, it would be almost impossible not to be exposed to pathogenic staphylococci. Other factors, therefore, must be sought after to explain why some women develop acute infections and others do not. Predisposing factors within the breast itself must provide favorable conditions for the invading organism to set up an inflammatory process.

Stagnant milk, like old blood and other deteriorating body tissues, is recognized as a good medium for promoting bacterial growth and infection. Walsh[14] was struck most forcibly by the significance of milk stagnation and termed it the "highest common factor" as related to breast infections. Stagnation is most prominent during early postpartum engorgement and the incidence of breast infection is common in the first two weeks' lactation, following which the incidence diminishes as the duration of lactation increases. Another similar period

of stagnation and infection is at the time of weaning, but it may occur at any time when there is interference with the proper emptying of the loaded breast. Newton and Newton[15, 16] and Waller[17] wrote extensively and thoroughly on the let-down reflex, a mechanism by which the mother actively expels the milk which is already in the breast in response to the stimulation of sucking. They pointed out that the reflex is extremely sensitive to emotional stimuli and can be inhibited by pain, emotional upheaval, or fear.[15, 17] In order to avoid stagnation due to improper functioning of this reflex, it seems wise not to allow or encourage breast feeding in patients who dislike, or who are indifferent or averse to, the procedure. On the other hand, in patients desirous of nursing, it is essential to help them avoid discomfort, embarrassment, emotional disturbances, and distractions both in the hospital and at home.

Bacteriology

A total of 99 breast abscess cultures were obtained in different patients, the results of which are shown in Table I. Of these, 96 were pure cultures and only 3 were mixed cultures. Of the pure cultures, 59 were hemolytic *Staphylococcus aureus,* coagulase positive, 36 were nonhemolytic *Staphylococcus aureus,* coagulase positive, and 1 was nonhemolytic *Staphylococcus albus,* coagulase positive. The mixed cultures consisted of:

1. Hemolytic *Staphylococcus aureus,* coagulase positive, paracolon and Pseudomonas.

2. Hemolytic *Staphylococcus aureus,* coagulase positive, beta hemolytic streptococcus (Enterococci).

3. Nonhemolytic *Staphylococcus aureus,* coagulase positive, and beta hemolytic streptococcus (Enterococci).

TABLE I. BREAST ABSCESS CULTURES

Pure cultures		96
Hemolytic *Staphylococcus aureus,* coagulase positive	59	
Nonhemolytic *Staphylococcus aureus,* coagulase positive	36	
Nonhemolytic *Staphylococcus albus,* coagulase positive	1	
Mixed cultures		3
Hemolytic *Staphylococcus aureus,* coagulase positive, paracolon, Pseudomonas	1	
Hemolytic *Staphylococcus aureus,* coagulase positive, beta hemolytic streptococcus (Enterococci)	1	
Nonhemolytic *Staphylococcus aureus,* coagulase positive, beta hemolytic streptococci (Enterococci)	1	
Total		99

It is seen that these organisms possess pathogenicity as indicated by the ability to hemolyze blood or to coagulate plasma,[18] and all of the staphylococcal organisms possessed one or the other of these factors or both.

Apparently, pathogenic staphylococci are the prime offenders, being found in all cultures with streptococci and coliform type organisms associated in only the 3 mixed cultures. Abscess attributable primarily to other bacteria (pneumococcus or gonococcus) and yeastlike organisms, as well as the streptococcus and coliform type, is not borne out by this study.

Antepartum and Postpartum Cultures.—These cultures were obtained from patients as they were admitted to the labor rooms and repeated on the same women on the day of discharge. Sixty patients were utilized, with a total of 119 cultures. As seen from Table II, 94 pure cultures of nonpathogenic nonhemolytic *Staphylococcus albus,* coagulase negative, were obtained. There were 5 mixed cultures of the same containing different nonpathogenic contaminants.

There were 14 other cases of nonpathogenic (avirulent) nonhemolytic *Staphylococcus aureus,* coagulase negative, and 2 with other avirulent contaminants. This leaves only 6 cultures of potentially pathogenic organisms (pure or mixed) which could be the source of future infection, 3 of which were found on antepartum cultures and 3 on postpartum cultures.

TABLE II. ANTEPARTUM AND POSTPARTUM CULTURES

Nonhemolytic *Staphylococcus albus,* coagulase positive		94
Nonhemolytic *Staphylococcus albus,* coagulase negative, plus other organisms:		
Diphtheroids	3	
Nonhemolytic streptococci	1	
Sarcinae	1	5
Nonhemolytic *Staphylococcus albus,* coagulase positive		2
Nonhemolytic *Staphylococcus aureus,* coagulase negative		12
Nonhemolytic *Staphylococcus aureus,* coagulase negative, plus other organisms:		
Alcaligenes faecalis	1	
Diphtheroids	1	2
Nonhemolytic *Staphylococcus aureus,* coagulase positive, plus other organisms:		
Alpha streptococcus	1	1
Hemolytic *Staphylococcus aureus,* coagulase negative, plus other organisms:		
Alpha streptococcus	1	1
Hemolytic *Staphylococcus aureus,* coagulase positive		2
Total		119

In comparing antepartum and postpartum cultures (Table III), in 16 patients the bacteriology of the breast was altered. All three of the potentially pathogenic antepartum organisms were found to have been replaced by benign organisms on the patient's discharge from the hospital. However, 3 postpartum pathogenic organisms were now found where previously benign ones had been present. Very little can be concluded from this, other than that hospital environment can eliminate as well as contribute pathogenic organisms. The remaining 10 cases of altered breast bacteriology were merely a replacement of benign with a different nonpathogenic organism or an acquisition or loss of an additional organism such as *Alcaligenes faecalis* (1 case), Sarcina (1 case), and diphtheroids (4 cases).

TABLE III. ANTEPARTUM AND POSTPARTUM CULTURES

Cultures Same Ante Partum and Post Partum.—		
39 pairs nonhemolytic *Staphylococcus albus,* coagulase negative	78	
2 pairs nonhemolytic *Staphylococcus aureus,* coagulase negative	4	82
Cultures Different Ante Partum and Post Partum.—*		
16 pairs	32	
Cultures—no check	5	37
Total		119

*For breakdown of cultures that were different ante partum and post partum, see text on "Antepartum and Postpartum Cultures."

In Vitro Sensitivity Determinations.—Specimens of pus cultured from 33 cases, consisting of 14 specimens of hemolytic *Staphylococcus aureus,* coagulase positive, and 19 of nonhemolytic *Staphylococcus aureus,* coagulase positive, were submitted to sensitivity tests against three antibiotics, penicillin, erythromycin, and tetracycline. Hemolytic *Staphylococcus aureus,* coagulase positive, was found to be moderately resistant or resistant to penicillin in 83 per cent, to tetracycline in 50 per cent, and to erythromycin in 7.7 per cent (Table IV).

Nonhemolytic *Staphylococcus aureus,* coagulase positive, similarly showed resistance in 94.7 per cent to penicillin, 18.7 per cent to tetracycline, but in no instance to erythromycin. The average figures for both organisms are: penicillin 88.8 per cent, tetracycline 34.4 per cent, erythromycin 3.9 per cent.

TABLE IV. IN VITRO SENSITIVITIES OF BREAST ABSCESS CULTURES (33 CASES TESTED AGAINST 3 ANTIBIOTICS)

HEMOLYTIC STAPHYLOCOCCUS AUREUS, COAGULASE POSITIVE	RESISTANCE	NONHEMOLYTIC STAPHYLOCOCCUS AUREUS, COAGULASE POSITIVE	RESISTANCE
Penicillin (units).—			
> 10 12 cases	83.0%	> 10 18 cases	94.7%
> 1.5 2 cases		> 1.5 1 case	
14		19	
Erythromycin (mcg.).—			
> 10 13 cases	7.7%	> 10 19 cases	0 %
> 50 1 case		> 50 0 cases	
14		19	
Tetracycline (mcg.).—			
> 10 7 cases	50.0%	> 10 16 cases	18.7%
> 50 7 cases		> 50 3 cases	
14		19	
Total tests	99		

Penicillin: > 10 means absolute resistance.
< 10 means varying degree of sensitivity.
Erythromycin and tetracycline:
> 50 means absolute resistance.
< 50 means varying degree of sensitivity.

Sawyer and Walker[19] found 87 per cent resistance of *Staphylococcus aureus* of breast abscess to penicillin, and 33 per cent to dihydrostreptomycin. There was no resistance to any of the following drugs, Aureomycin, Terramycin, Chloromycetin, and bacitracin, in which 100 per cent sensitivity was noted.

Walsh[14] in 1949 obtained results quite the opposite of the above, wherein 51 of 57 cultures of coagulase-positive *Staphylococcus aureus* were sensitive to penicillin, giving a resistance rate of 10.5 per cent.

Martyn,[13] also in 1949, examined cultures from the nasopharynx of 130 newborn babies and found a 50 per cent carrier rate of coagulase-positive staphylococcus, of which 55 per cent were penicillin resistant, but only 3.7 per cent streptomycin resistant.

In Vivo (Clinical) Response to Antibiotics.—Seventy cases were treated with penicillin alone. In 17 of these adequate response was not achieved and we, therefore, switched to Dicrysticin (14 cases) and Achromycin (3 cases). Primarily, penicillin alone was effective in 75.7 per cent of the cases. Disparity between this result and the in vitro sensitivity of 11.2 per cent is evident. Due to various factors, clinical response does not always correspond to in vitro results. A good clinical response may occur with an organism reported as resistant and vice versa. Again, organisms resistant to set standards of levels of testing in the laboratory may respond to large doses of antibiotics clinically.

Dicrysticin was used primarily in 58 cases and secondarily in 14 cases, a total of 72 cases. It was found noneffective in only one instance of the secondary group, therefore the total percentage value was 98.6. We can conclude that penicillin in conjunction with streptomycin as Dicrysticin (or Combiotic) is more potent in controlling *Staphylococcus aureus* than penicillin alone. All cases responded to Achromycin (5 cases) or Terramycin (4 cases).

Interestingly, no antibiotic was used in 10 cases. These patients were afebrile on admission, with well-advanced and localized abscesses. They remained afebrile and the infective process resolved without further complications. Here, other factors in therapy as well as body defense mechanisms have to be taken into consideration. This could also explain the more favorable in vivo response to antibiotics as compared to the in vitro results.

The seemingly high per cent of resistance to antibiotics, especially penicillin, is not surprising since pathogenic staphylococci are capable of producing through mutation different strains of organisms in very short periods of time, calculated to be as short as 20 minutes.

Treatment

On admission the patients were placed on antibiotics, and measures to relieve pain or discomfort by analgesia were initiated. If ready, the abscesses were surgically drained the next morning. Penicillin was administered intramuscularly in doses of 600,000 units once or twice daily thereafter. Of the 70 cases in which it was used, clinical response of value was found in 75.7 per cent. Dicrysticin, ampule twice a day, proved more effective (98.6 per cent), failure to respond occurring in only one case. Achromycin or Terramycin in 250 mg. doses four times daily was employed in 9 cases (the former in 5 cases, the latter in 4), with good results. Colbeck[2] advised that in the presence of an outbreak of breast abscesses the infants should receive either local or general treatment with the appropriate antibiotic, with the object of eliminating nasopharyngeal infection.

Surgical procedures were performed, with Seconal and opiates as premedication, and self-administered Trimar inhalations. Three methods of incision are recognized: (1) Single or multiple incisions extending radially in line with the duct from the areola over the abscess area. The abscess locules are then disrupted by finger dissection, liberating the purulent material. The cavities are irrigated with sterile water and packed with iodoform gauze. (2) When the abscess is located in the upper portion of the breast, the procedure is similar except, in addition, a small secondary stab wound is made in the lower dependent portion of the breast and a drain guided through it from the abscess region. The primary incision over the abscess is closed with interrupted sutures. (3) An incision is placed exactly along the margin of the areola (Walsh[14] suggests 1 cm. as adequate), through the skin and subcutaneous tissue but not entering the ducts. By careful blunt dissection, preferably with a hemostat, the compartment of the breast involved is entered. The adjacent compartments are opened by the same procedure by traversing the original cavity through the same incision. A small rubber drain is inserted and allowed to remain in place until drainage is completed. Proponents of this method favor it over the other two techniques because it supposedly does away with the long disfiguring scar and avoids the possibility of secondary infection. We preferred to use method No. 1 or No. 2 primarily, because the wide extent of the lesions required a more radical approach for adequate evacuation and subsequent drainage. Circumareolar incision and drainage is more suited to lesions limited to less than a quarter segment of the breast, whereas the majority of ours involved more than one-third of the breast. The objection to the second method is that healthy breast tissue is exposed to purulent material with risk of invasion by the offending staphylococcus. We have been impressed by the manner in which the cavity is filled with granulation tissue, the skin edges healing with an amazingly fine scar, and the breast recovering its natural form. Deformity of the breast occurred in only 2 instances, both with extreme degrees of destruction; in one the skin had sloughed over a large segment of the breast and skin grafting was required.

Practically all of the abscesses were advanced and obvious. Some cases were encountered, however, in which no fluctuation or definite evidence of pus could be detected, but where the breast displayed an inflamed, indurated zone. We concur with Walsh[14] that one should not wait for the appearance of fluctuation, for the abscess has often reached a considerable size before fluctuation is evident, depending to some extent on its depth. Any area of tense induration in an inflamed breast should be regarded as containing pus and drained accordingly.

Postoperative Care

On completion of operation the breast is covered with sterile gauze and supported by a breast binder. The latter has a twofold purpose; it gives greater comfort to the patient and aids in drying up the milk.

Daily thereafter the dressings are changed. The iodoform gauze pack is removed over a period of the next one to three days, depending on the amount used. In the early part of the series the cavity was irrigated with 50 per cent Dakin's solution. Later this was supplanted by Varidase, used in two forms: (1) 25,000 units in solution in sterile water introduced daily following irrigation with normal saline (Dakin's solution interferes with the action of the Varidase); (3) incorporated into a jelly and applied to the surface of wound with the gloved finger. Varidase in jelly gave excellent results, promoting a more rapid appearance of a cleanly granulating wound, with early elimination of necrotic slough and discharge. Closer application and maintenance of Varidase by jelly on the tissues would account for its more potent action than when allowed to flow about in the cavity, with a large proportion escaping through the wound.

Walsh advocated perpetuation of lactation, whereby the patient manually expresses the milk from the infected breast. This milk is subsequently boiled and fed to the infant. In 84 cases where this boiled milk was fed to babies, not one developed gastroenteritis. Taylor and Way[20] allowed the infant to nurse directly from the infected breast and reported that no baby in their series developed gastroenteritis. However, Colbeck reported 10 cases in which children of mothers with breast abscess died of lung abscess, probably due to aspiration of infected milk. He suggested that this may be a possible explanation when babies die suddenly of an unknown cause.

In Walsh's series of 45 cases, great care was taken to prevent retention of milk, and lactation was encouraged rather than inhibited. It seems contrary to all surgical principles, however, to "massage" an infected mass. In none of these 45 cases did a secondary abscess develop. In 12 other cases, where no particular care was taken to avoid milk retention, 3 patients developed a secondary abscess in the axillary tail. Secondary surgical intervention was required in 26 of our cases wherein we had utilized measures (hormones and binder) to dry up the breast. Some of these were planned as secondary when areas of induration did not appear to be ready for surgical drainage at the original procedure. Others developed adjacent to the primary site, especially when inadequate surgery was performed on extensive lesions, or when method No. 2 or No. 3 was utilized. However, no secondary abscesses were recorded in the axillary tail. It is doubtful if the infected breast actively secretes milk, as all damaged tissue is put to rest by Nature. The breast can be emptied at the time of operation and kept functionless by hormones and binder. This would be the procedure of choice, although there are instances in which lactation has subsided and breast infection has occurred and gone on to suppuration. Heat in the form of radiation or compresses and mild analgesic drugs are helpful in promoting the comfort of the patient.

These procedures are continued until the patient is afebrile, the wound granulating and clean, and the breast is soft, with resolution of induration. The patient is then discharged from hospital care and is followed at home by a Visiting Nurse every two days, and seen weekly in the clinic.

Results of Therapy

Temperatures as high as 105° F. on admission usually dropped to normal within 24 hours after incision and drainage, and associated antibiotic therapy. The patients who continued to run a febrile course, or subsequently to have a spiking temperature, required redisruption of locules resulting from an inadequate original procedure or the development of new pockets. This proved to be the case in 26 instances. Fortification or change of antibiotic from penicillin was necessary on occasion to abate the infection and enhance response to the surgical treatment.

The average postoperative duration of hospitalization was 6 to 7 days, the shortest being 2 days and the longest 19 days. Prolonged institutional care was necessary in cases in which practically the whole breast was involved, requiring two to three quadrant incisions to produce proper disruption of the locules and evacuation of purulent material.

The patients were followed in the clinic at weekly intervals for 3 to 10 weeks before healing was complete. The end results of wide incisions were fine scars and healing with minimal distortion of the breast in an insignificant number of cases.

Summary

The mechanism of breast infection is most likely one in which the infant acquires the pathogenic staphylococcus either in the hospital or home environment and transmits it to the breast upon suckling. Under favorable conditions of milk stasis, retrograde invasion of the duct occurs and an inflammatory process is initiated which may progress to abscess formation. Since the average duration of symptoms was 7.7 days before the patients sought medical care, personalized postpartum instruction to nursing mothers seems essential. This would permit earlier awareness of breast abnormality and allow for prompt antibiotic therapy in order to circumvent abscess formation. Infants who exhibit signs of upper respiratory infection should be removed from the breast, isolated (manual emptying of breasts instituted temporarily), and receive proper antibiotic care. In such cases the two conditions apparently necessary for promoting breast infection are present: (a) inability of sick infants to feed well with resultant ineffectual emptying of breasts, thereby promoting stasis and stagnation, and (b) the presence of a pathogenic organism in the upper respiratory tract of the infant.

Infants of mothers who display breast infection should be placed in the isolation nursery and given antibiotic treatment. In smaller hospitals, when mastitis appears on the maternity floor, it would be feasible to administer antibiotics prophylactically to all infants in an attempt to prevent cross infection. At Cook County Hospital this practice would be virtually impossible. All normal postpartum patients leave the institution within 48 to 72 hours of delivery, long before signs and symptoms of infection are manifested. Also, the distribution of drugs to infants numbering in excess of 1,200 per month is in itself a prohibitive procedure. The ultimate but drastic measure for prevention

of breast infection would be to eliminate all breast feeding during periods of increased breast infection. Breast feeding could be resumed when the infection has been curtailed.

This protracted series of augmented numbers of breast infections would indicate that more than an "outbreak" has occurred. It is more plausible that a new norm or standard of bacterial virulence has been established, which is refractory to the more commonly used antibiotics, particularly penicillin.

Conclusions

1. The incidence of breast abscess at Cook County Hospital has markedly increased in frequency during the past two years.

2. The main organism isolated in this series was pathogenic *Staphylococcus aureus*. Occasional nonpathogenic contaminants also were present.

3. Although penicillin in large dosage apparently showed good clinical response in 75.7 per cent of the cases, sensitivity tests (88.8 per cent resistance to penicillin) would indicate that penicillin therapy is of little or no value. Other drugs, Dicrysticin, streptomycin, Achromycin, or Terramycin, would offer more hope in combating and controlling breast abscess.

4. Varidase incorporated into jelly and applied directly to the wound promotes rapid elimination of necrotic slough and discharge, promoting a clean, readily granulating wound.

5. Routine cultures on admission and discharge of patients indicate that hospital contamination is no more a source of infection than nonhospital environment. Three patients who were admitted with potentially pathogenic organisms showed benign organisms on discharge, while 3 patients who entered with benign organisms acquired potentially pathogenic organisms.

6. Early incision and drainage are imperative. Inflamed, indurated areas should be incised before fluctuation or other signs of purulent content of the abscess are discernible.

7. The type of incision depends on the extent of the lesion. If less than a quarter segment of the breast is involved, circumareolar incision will suffice; otherwise an extensive radial incision or multiple incisions, if necessary, should be employed.

8. Preventive measures are discussed.

References

1. Sherman, Alfred J.: Obst. & Gynec. **7**: 268, 1956.
2. Colbeck, J. C.: Canad. M. A. J. **61**: 557, 1949.
3. Knott, F. A., and Blaikley, J. B.: J. Obst. & Gynaec. Brit. Emp. **51**: 386, 1944.
4. Hobbs, B. C.: Bull. Hyg. **19**: 391, 1944. (Abstract.)
5. Pyle, L. R.: Am. J. Obst. & Gynec. **55**: 676, 1948.
6. McGuinness, F. G., and Musgrove, G. S.: Canad. M. A. J. **61**: 356, 1949.
7. Gibberd, G. F.: Am. J. Obst. & Gynec. **65**: 1038, 1953.
8. Martin, T. B. M., and Whitehead, J. E. M.: Brit. M. J. **1**: 173, 1949.
9. Williams, R. E. O.: J. Path. & Bact. **58**: 529, 1946.
10. Matthews, E., Atkinson, H. F., Saunsbury, P. T., and Clegg, H. W.: Brit. M. J. **1**: 54, 1949.
11. Duncan, J. T., and Walker, J. J.: J. Hyg. **42**: 474, 1942.
12. Torrey, J. C., and Reese, M. K.: Am. J. Dis. Child. **69**: 208, 1945.
13. Martyn, G.: Brit. M. J. **1**: 710, 1949.
14. Walsh, Anthony: Lancet **2**: 635, 1949.
15. Newton, M., and Newton, N. R.: Surg., Gynec. & Obst. **91**: 651, 1950.

16. Newton, M., and Newton, N. R.: J. Pediat. 33: 698, 1948.
17. Waller, H. K.: Lancet 1: 69, 1943.
18. Wilson, G. S., and Miles, A. A.: Topley and Wilson's Principles of Bacteriology and Immunity, ed. 4, London, 1955, Edward Arnold & Co., vol. 1, p. 715.
19. Sawyer, C. D., and Walker, P. H.: Surg., Gynec. & Obst. 99: 368, 1954.
20. Taylor, M. D., and Way, S.: Brit. M. J. 2: 731, 1946.

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Discussion

DR. DONALD DYE.—The interesting increasing incidence at the Cook County Hospital and the Philadelphia General Hospital, when compared with the nonincreasing and low incidence on the home delivery and care service of the Chicago Maternity Center (Table I), leaves one to wonder if perhaps there are not some factors not explored in this study which might account for the relative variance. It has long been stated and recognized that the occurrence of mastitis could be prevented by prophylactic measures. Previously much attention has been directed to the prevention and treatment of fissured nipples. In the series presented tonight fissuring of the nipples and antecedent trauma seem to play no significant role. In the light of previous studies should not prophylaxis be otherwise instituted?

Table I. Comparative Incidence (%) of Breast Abscesses

	1951	1952	1953	1954	1955	5 year total
Chicago Maternity Center	0.21	0.20	0.19	0.35	0.14	0.22
Cook County Hospital	0.14	0.18	0.34	1.13	1.35	0.63
Philadelphia General Hospital	0.39	0.79	1.19	1.28	0.82	0.89

The authors have shown no significant contamination of the outer breast but have otherwise failed to further their studies. This might well prove interesting and informative.

The normally high incidence of *Staph. aureus* in the normal healthy population and the lack of suitable means of differentiating specific strains, until recently, seriously hampered investigation. Recent refined bacteriophage typing has made such studies possible. Sherman in his study of staphylococci in attending personnel has shown 53.2 per cent to be carriers. This compares with 32.2 per cent of patients on admission to the hospital. Of the attending personnel so studied, the highest incidence, 53.8 per cent, appeared among the nursing staff. The greatest single reservoir was found to be the nasopharynx. Seventy-seven and four-tenths per cent of the strains so isolated were found to be penicillin resistant. This compares with 28.5 per cent of the nonhospital strains. They further showed that coagulase positive staphylococci were isolated from the nasopharynx in but 9.7 per cent of infants at 12 to 24 hours of age and in 20 per cent at 72 hours of age. Similar findings and conclusions came from a study during an epidemic of staphylococcus infections among infants and nursing mothers at the Ohio State University Hospital early last year.

Ravenholt and LaVeck in a study conducted in the Seattle area presented most interesting findings. They, as do others, consider staphylococcal disease relatively unknown, or at least uncommon, until January of 1955. In March of 1955 a new mother died of septicemia secondary to a breast abscess. They investigated the combined problems of skin infections in the newborn and breast abscesses in the mother. In their study the median interval from delivery to onset of illness was 8 days in infants and 14 days in mothers. The relationship of epidemic curves for infant and maternal illnesses suggests the precedence of infant illnesses. This concept of primary infection in the infant and secondary infection in the mother was fortified by additional findings. In the 34 families wherein both mother and infant had suppurative illnesses, the onset of the illness in the infant preceded that in the mother in 26 cases, or 76 per cent. Eighteen of the 19 mothers

who developed breast abscesses nursed their infants. The conductors of this study believed that they could show a decrease in breast abscesses in mothers discharged on the day of delivery or the first postpartum day!

These variances seem to be statistically significant. With the findings of penicillin-resistant causative organisms in 88.8 per cent of this series, should we not seek further hospital correlation rather than deny it? In the series presented here tonight, nipple cultures from 60 patients produced but 6 positive staphylococcus cultures. But 3 of these were coagulase positive. Cultures of the abscesses, however, produced a preponderance of these organisms. It appears that the patient's immediate environment was not contaminated by these organisms. So, once again, perhaps the hospital, perhaps by way of its personnel, has given to the baby these organisms (even during the usual 3 day stay at the Cook County Hospital) and the babies have introduced the organisms into the patients' breasts through suckling. The presence of a plentiful and a rather permanent source of infection (contaminated environment and carrier personnel) and production and exposure of an inexhaustible supply of susceptible newborn infants permit easy propagation. The treatment afforded these patients admitted to the Cook County Service seems to be most adequate. Is it really so surprising that the clinical response and the in vitro sensitivities do not necessarily correspond? Regardless of the use of antibiotics (and in days prior to their usage) did not abscesses cure themselves after spontaneous rupture or wide incision and drainage?

It appears that the authors' conclusion that hospital contamination is no more a source of infection than the nonhospital environment, in view of previous studies, is to be questioned. The baby as a possible and probable source of transmission has been ignored. The relatively stable and low incidence at the Chicago Maternity Center may further suggest the possibility of a hospital-offered organism.

DR. VARGA (Closing).—It is remarkable that the percentage of breast abscesses recorded in patients delivered by the Chicago Maternity Center over the 5 year period outlined by Dr. Dye should be only half as great as that encountered at Cook County Hospital. This is in keeping with the view that hospital environment is the main source of infection in this condition. Moreover, it suggests that a return to home deliveries might be desirable in order to avoid breast infection; or, on the other hand, a preference for prolonged postpartum hospitalization, so that incipient infection can be recognized and treated. However, we included in our series abscesses which developed in patients delivered at home without medical assistance, and others who were delivered by the personnel from the Chicago Maternity Center. I assume that all of these latter cases have been included in their series. Deletion of these from our large number of cases would alter our statistics very little, whereas the addition of these cases would materially increase Maternity Center's average figure to a degree proportionate to ours.

The need for our apparently radical surgical approach has been questioned and a more conservative method of incision and drainage suggested. We outlined the technique of circumareolar incision as applicable to smaller, well-localized lesions. Failure in some of our earlier cases could be related to inadequacy in the extent of incision, interfering with accessibility to some of the involved locules, thus necessitating subsequent reopening of the wound. I wish to re-emphasize that the majority of our patients delayed in seeking medical care and when first seen had involvement in more than half of the breast. The numerous affected locules cannot be reached via a miniature incision. As long as pus is retained in one locule the signs and symptoms will not abate, and the disease may progress to involve adjacent areas of unaffected breast tissue.

Our bacteriologic studies would have been more complete had we included cultures obtained from the nasopharynx of a comparable number of hospital personnel and newborn infants. Perhaps this might be attempted in the near future. It has been established by many authors, however, that hospital personnel do have a higher incidence of pathogenic organisms in their environment. It is evident also that newborn infants soon harbor similar organisms. The important factor relevant to breast infection is the transmission of these organisms to the healthy lactating breast.

CEREBRAL VASCULAR ACCIDENTS IN PREGNANCY*

Report of Six Cases Without Eclampsia: Two Spontaneous Subarachnoid Hemorrhages and Four Cerebral Thromboses

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CEREBRAL vascular accidents in pregnancy may be due to either hemorrhage or thrombosis. The obstetrician is cognizant of these complications during pregnancy because some of the underlying factors, namely, increased fibrin (up to 40 per cent, at term[18]), anemia, and increased blood volume,[24] that favor either thrombosis or hemorrhage are present during pregnancy, and the same age factor too is common to all three conditions.

Ullery[27] states that throughout the history of childbirth physicians have been acutely aware of the tendencies toward hemorrhage and thrombosis during pregnancy, labor, and the puerperium. The exact mechanism of intravascular clotting and venous thrombosis is unknown. Many theories have been advanced, but none has been completely acceptable in answering all the problems of coagulation in the human body. Extensive research has shown the clinical and physical properties of in vitro clotting to be well understood, but in vivo intravascular clotting still remains an enigma. Stefanini,[25] in 1953, reported that most investigators are in accord on certain principles of coagulation mechanisms. From Quick's[19] diagrams and presentations he stated it may be seen that the platelets and the plasma are the two main constituents of the blood that produce fibrin or coagulation in the presence of disease, injury, or abnormality of the vascular endothelium. The vital step in the mechanism is the production of thrombin. No formation of thrombin takes place until free thromboplastin becomes available. When platelets adhere to the surface of the abnormal endothelium they rupture or disintegrate and liberate thromboplastinogenase, which activates the thromboplastinogen of the plasma to form thromboplastin. The action of the thromboplastin on the prothrombin complex of the plasma forms thrombin. Thrombin then combines with fibrinogen to form fibrin, the end product of coagulation.

When the route of dissemination of emboli is studied, as demonstrated by Batson[1] in 1940, who injected Lipiodol into the pelvic veins and showed a communication to the cerebral vessels by way of the vertebral veins, it becomes easy enough to understand secondary thrombotic (metastatic) phenomena in cerebral vessels from thrombophlebitis originating in the pelvis, but the susceptibility of these vessels to spontaneous thrombotic processes has not yet been satisfactorily explained.

Wilson's[31] recent neurology text, in speaking of etiology, states that thrombosis is frequently associated with disease of the vessel walls, for example

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atheroma, or the arteritis of syphilis or other infectious conditions. In the absence of vascular lesions, it is commonly ascribed to increased coagulability of the blood, for instance, in hemic states, during pregnancy and the puerperium. Stagnation of viscous blood, lowered blood pressure, and reflex paralysis of vasomotor origin have also been implicated.

Cerebral hemorrhage, on the other hand, may be due to varied and sundry factors, any or all of which may be acting in a minor role, but Walton[28] reported that 80 per cent of all spontaneous subarachnoid hemorrhages, in the absence of eclampsia, arise through rupture of an intracranial aneurysm, another 10 per cent through bleeding from an angioma, and in the remainder many pathological conditions may be implicated.

As for the age factor, Descher and Rowe[6] found that spontaneous subarachnoid hemorrhage may occur at any age, but is perhaps most common in early adult life so that it may occasionally complicate pregnancy and labor. Walton felt that the incidence of subarachnoid hemorrhage in pregnant women is no greater than in the general population.

Wilson cited Alpers and Palmer, who in 1929 found cerebral hemorrhage more frequent than cerebral occlusion during pregnancy, although thrombosis of cerebral veins and sinuses is not particularly rare.

Gerin-Rose,[11] in 1859, described the first case of subarachnoid hemorrhage during pregnancy and very few cases have been reported until recent years. Lazard,[15] in 1899, reported a case of cerebral hemorrhage arising during labor (probably the first in the American literature). Weigle[30] wrote that cerebral hemorrhage, oftentimes with extension into the subarachnoid space, has been noted frequently in patients with eclampsia[4, 14] and toxemia.[17, 26] Conley and Rand[3] also commented upon the relative infrequency of the spontaneous subarachnoid hemorrhage, while many such hemorrhages are encountered in women with eclampsia. They added further that, in reviewing the experience of other authors, they realized that it has been difficult for them to exclude some cases of borderline toxemia when reporting on this complication of pregnancy. In rare instances, as reported by Richardson and Hyland,[20] the two conditions may occur simultaneously. Eller,[9] quoted by Conley and Rand, in 1946, while discussing the problem of cerebrovascular complications of pregnancy, pointed out that all patients with fatal hemorrhage and softening of the brain, even in the presence of hypertension, albuminuria, and convulsions, are not necessarily eclamptic.

Schwartz,[23] in 1951, stated that the apoplectic onset of headache and coma in a relatively young woman with or without hypertension, associated with a grossly bloody spinal fluid, is pathognomonic of subarachnoid hemorrhage. More often than not, a pregnant woman with these symptoms first has a diagnosis of toxemia of pregnancy, until further work-up or the findings at the autopsy table show the correct diagnosis. Although hypertension, albuminuria, headaches, convulsions, and coma are common to both conditions, grossly bloody spinal fluid does not occur in eclamptic toxemia, no matter how severe the toxemia.

Walton stated that subarachnoid hemorrhage complicating pregnancy may pose important problems of management and, as Mackenzie[16] has pointed out, diagnostic difficulties may arise, since irritation of the hypothalamus by subarachnoid blood may produce hypertension and albuminuria. These observations have inspired the view that generalized vascular changes are usually responsible for subarachnoid hemorrhage in pregnancy, labor, or the puerperium. While this is true in many cases, it is now evident that subarachnoid hemorrhage of aneurysmal or angiomal origin occasionally complicates an otherwise normal pregnancy. Of the 312 cases of spontaneous subarachnoid hemorrhage reported by Walton, only two occurred during pregnancy. In a total of 15,417 deliveries,

de Carle,[4] in 1949, found subarachnoid hemorrhage had occurred in 15 patients with eclampsia, while in only 3 cases was it a complication of otherwise normal pregnancy.

Bristowe,[2] in 1888, reported the first case of cerebral thrombosis in a woman 6 weeks pregnant, confirmed at autopsy. Dowie,[7] writing in the *British Medical Journal,* stated that the latter was the only case he could find in the available literature; he stated further that, although cerebral thrombosis in pregnancy is rare, there are many cases described of its occurrence during the puerperium. Dereaux and Dereaux[5] stated in 1955 that, while there are numerous cases of cerebral thrombosis reported in the French literature occurring in the puerperium and postabortion period, there was no other case than the one they reported in detail, and verified by autopsy, which occurred during pregnancy.

The symptoms of the two conditions, cerebral hemorrhage and occlusion, vary but little, and each is dependent upon the location, the size of the vessel, the areas involved, the rapidity of the increase in intracranial pressure. Kendall[13] reported that headaches, convulsive phenomena, localized cerebral lesions, raised intracranial pressure, and disturbance of speech are indicative of a vascular accident. Conley and Rand related that almost without exception the patient is seized with severe headache, usually in the occipital region. This may be accompanied by nausea and vomiting, derangement of the conscious state, which varies from confusion to coma, depending upon the degree of extravasation, motor paralysis, and, not infrequently, convulsions.

The diagnosis, both direct and differential, of these two conditions is dependent upon spinal puncture. The presence of blood, which may have originated in the meninges or extended from the brain into the ventricles or subarachnoid space is the sine qua non upon which the diagnosis of subarachnoid hemorrhage rests. Wilson summarizes the diagnostic principles of occlusion as follows: (1) sudden or rapid development of general cerebral symptoms in morbid states where venous or sinus thrombosis is a possibility suggests its actual occurrence; (2) the diagnosis is confirmed when external signs begin to show.

Cerebral angiography as pioneered by Egas Moniz[8] offers an effective approach to localization of the hemorrhagic lesion, and Feldman and associates[10] state: "The location of the aneurysm must first be accurately established . . . and the competency of the communicating arteries in providing an adequate blood supply to the brain must also be ascertained." The method of obtaining this information does not differ from that in the nonpregnant state. The optimum time for cerebral angiography will depend upon the total appraisal of the patient. Wechsler and Gross[29] believe that all women without eclampsia as well as those with borderline eclampsia who are victims of spontaneous subarachnoid hemorrhage should have the benefit of cerebral angiography because it offers the only reliable means of demonstrating the source of the hemorrhage.

The mortality rate of subarachnoid hemorrhage caused by rupture of an intracranial aneurysm is high, even without the added factors introduced by pregnancy and labor. According to Rhoades,[21] about 50 per cent of all cases of ruptured intracranial aneurysms end fatally. Schreiber[22] claimed that one third die during the first admission and, of those who survive the first week, one half have recurrences. In the 20 cases of spontaneous subarachnoid hemorrhage complicating pregnancy without eclampsia collected from the literature, to which Conley and Rand added 8 cases of their own, the maternal mortality was 42.9 per cent, while that of the fetus was 26.3 per cent, although in 4 of the 28 cases no mention was made of the fate of the baby.

The length of gestation and the imminence of labor with its associated stress and strain superimposed upon an already potentially disastrous aneurysm obviously add to the gravity of this explosive complication.

Wechsler stated that 30 per cent of all patients with cerebral hemorrhage die within the first 24 hours, 60 per cent within the first week, and 80 per cent in the first month. Less than half the number die of thrombosis within the first week, but the percentage is the same as for hemorrhage within the month.[12]

According to Wilson the prognosis of cerebral thrombosis depends chiefly upon: (1) the particular vessel damaged, (2) the age of the patient, and (3) severity of the attack. To these must be added the period of gestation and the imminence of labor with its consequent stress and strain. Certain ominous signs portend danger: the more extensive the softened cerebral area, the graver the outlook; deep and prolonged coma, too, suggests a course likely to be unfavorable; as in the case of cerebral hemorrhage, disordered heart action or breathing also signifies disaster.

The pathological findings in thrombosis are occlusion, either complete or incomplete, with necrosis of brain tissue locally, and distal effects depending upon the cerebral area involved; the morbid process for hemorrhage is the same as for hemorrhage from aneurysm or angiomas elsewhere.

Once the diagnosis is established the treatment is unequivocal; first and foremost, control of the bleeding in cerebral hemorrhage is mandatory; second, prevention of extension of the process; third, prevention of factors which might conceivably precipitate further or repeated episodes; then, last, attention should be directed toward the pregnancy. The principles for controlling cerebral hemorrhage in pregnancy do not differ from those in the nonpregnant state. Wilson states that, short of surgical procedures, inability to reach the ruptured vessel compels resort to an indirect approach. Absolute bed rest in the recumbent position with the neck free and the head somewhat raised and turned to the side to avoid obstruction from the tongue is required; lifting and moving are prohibited, save as may be imperative. Warmth and catharsis to lower blood pressure are advised. Lumbar puncture is often considered the best means of reducing intracranial pressure and thus promoting cessation of bleeding. Hypertonic glucose solutions may also be of benefit. To these one should add sedation as necessary to relieve strain, and oxygen and general supportive measures with complete disregard for the pregnancy, unless delivery is imminent and the added strain of an otherwise exhaustive labor might create a greater hazard to an already jeopardized mother. Walton stated that, if an attack of subarachnoid hemorrhage begins during labor, alleviation of physical strain is an urgent matter; in selected cases, depending upon the stage of labor, emergency cesarean section or instrumental delivery will be indicated before adequate treatment of the subarachnoid hemorrhage, or even of cerebral thrombosis, whether conservative or surgical, can be implemented. Occasionally, cesarean section must be employed to save the life of the child. During pregnancy or the puerperium, however, it is usually wise that each patient be treated as would any other with a cerebral vascular accident, be it hemorrhage or thrombosis.

Since the introduction of anticoagulants the treatment of thrombophlebitis regardless of location is directed toward stopping the spread or extension of the crippling lesion. Here again, nearness to the date of delivery alters the specific treatment. Because of the certain and marked delay in coagulation time, imminent delivery emphatically contraindicates the use of anticoagulants. With delivery one month or more away it seems perfectly safe to employ this most valuable aid, and I strongly advocate its use. Otherwise, with delivery imminent, the principles of treatment for cerebral thrombophlebitis are essentially the same as in cerebral hemorrhage, with the same consideration for reducing strain to a minimum, by means of proper sedation, judicious instrumental delivery, or cesarean section.

As soon as the immediate effects of the accident are over, then the same consideration for both the continuation of the pregnancy and the mode of delivery confronts the obstetrician. It becomes a question of the type of procedure that will produce the least possible strain to an already overburdened system. In general, it appears that pregnancy in the first trimester should be interrupted as soon as the patient has recovered sufficiently to tolerate the operative procedure, and that pregnancy in the second and third trimesters is best allowed to continue to term.

We feel that most of these patients do very well with heavy sedation in the first stage of labor and forceps extraction under inhalation anesthesia to relieve the strain of the second stage, and we reserve cesarean section for patients who exhibit too much delay in progress.

Most authorities are in accord that future pregnancies are to be prevented, preferably by sterilization, because repeated pregnancies would tend to place the patient in added jeopardy.

Case Reports

CASE 1.—*Spontaneous subarachnoid hemorrhage with recovery and instrumental delivery of a live baby at term.*

D. W., a 21-year-old Negro gravida ii, para i, entered the hospital on Jan. 4, 1954, because of intractable vomiting, inability to speak, and a paralyzed right side. The husband stated that his wife was perfectly well when he left his home at 7 o'clock in the morning. At 9:30 A.M., during a telephone conversation with a friend, she became suddenly aware of a weakness of the right side and she fell to the floor, where she was found by the friend who had become alarmed at the patient's inability to respond.

The past history disclosed a normal uneventful pregnancy terminating in a normal 6 hour labor at term in 1951. In addition, it was reported that the patient had suffered a mild attack of poliomyelitis at the age of 3 years.

At the initial examination she was described as a very lethargic woman who yawned frequently, was sweating profusely, showed marked inattention, but responded to verbal stimuli. She did not speak other than to move her lips and she seemed annoyed and irritated at her inability to utter words. The blood pressure was 90/52, the pupils reacted to light, and funduscopic examination revealed normal fundi. No sensory loss was present, but there were nuchal stiffness and spastic paralysis of the right upper extremity as well as of the right lower extremity. The abdomen was enlarged, approximately to the size of a 6 months' pregnancy with a fetus in the cephalic presentation and audible fetal heart tones. Lumbar puncture showed a pressure of 220 mm. of water with grossly and uniformly bloody spinal fluid. The Pandy reaction was 4 plus. The red blood count was 4.07 million, the hemoglobin 8 Gm. per 100 c.c. The serological test for syphilis was negative and the urine showed no albumin or sugar. The neurological diagnosis was spontaneous subarachnoid hemorrhage. She responded rapidly and satisfactorily to a regime of general supportive treatment, and by Jan. 18, 1954, she was found to have a full range of passive motion in the right upper extremity; she was able to take a few steps, her speech was improving rapidly, and she was discharged to continue physiotherapy at home.

On March 15, 1954, three months after the cerebrovascular accident, she re-entered the hospital, and walked unassisted to the admitting room where she was found to be in active labor. At 4 cm. dilatation she was given morphine sulfate, 1/6 grain, scopolamine, 1/150 grain for analgesia, and 2 hours later with complete dilatation she was delivered by means of forceps at the outlet under cyclopropane inhalation anesthesia. She and her new baby were discharged on the fifth postpartum day, at which time she displayed only a minimum residual right hemiparesis.

CASE 2.—*Cerebral hemorrhage from a ruptured aneurysm with recovery and normal delivery of a living child at term.*

M. B., a 41-year-old Negro gravida vii, para v, was admitted to the hospital on April 8, 1955, in deep coma. Her last menstrual period had occurred on Dec. 29, 1954, and the expected date of confinement was Oct. 5, 1955. Her prenatal course to date had been uneventful. Her mother stated that the patient had suffered a severe headache early on the morning of admission, followed by a sudden loss of consciousness and since then had had several attacks of convulsions.

Pertinent findings were coma, blood pressure of 126/84, temperature of 100.4° F., pulse 84, and respirations 22. The pupils were constricted and fixed to light, there were a flaccid paralysis of the left upper extremity, spastic paralysis of the left lower extremity, absence of abdominal reflexes, anesthesia of the entire left side. The eye grounds showed normal discs. The uterus was enlarged to the size of a 3½ months' pregnancy.

Lumbar puncture showed an initial pressure of 340 mm. of water and the spinal fluid was strongly bloody. The erythrocyte count was 4.14 million, hemoglobin 12 Gm., serological test for syphilis negative, urine analysis negative, and the blood chemistry within physiological limits.

A diagnosis of a lesion of the brain stem and geniculate body (probably aneurysm with leakage) was made. The condition seemed desperate and the prognosis for recovery very poor. A second spinal puncture on the fourth day showed a pressure of 330 mm., and the spinal fluid still bloody. On the eighth day the procedure was repeated and the pressure had diminished to 120 mm. and the fluid was now clear.

Improvement from this point progressed rapidly, the patient becoming mentally clear and completely oriented. Muscular recovery, however, was slow and some residual paralysis persists even at the time of this writing. An extremely disturbing external strabismus (outward deviation of the right eye) developed which necessitated mechanical occlusion by means of an eye patch, and that, too, has persisted to date.

On Sept. 26, 1955, she was re-admitted to the hospital at term, in active labor. The blood pressure was 112/68, pulse 100, respirations 24, and the temperature 98.6° F.

She was given morphine sulfate, ⅙ grain, and scopolamine, 1/150 grain, at 4 cm. dilatation. Three hours later she was delivered normally of a living child under cyclopropane anesthesia. She was discharged on the seventh postpartum day with considerable motor recovery of the upper extremities, enough to wash her face, comb her hair, feed herself, and hold her baby securely. She was unable to walk but could take a few steps unassisted.

CASE 3.—*Cerebral thrombophlebitis, recovery with marked residual, and repeat pregnancy with normal delivery of a living child, 14 months after cerebral vascular accident.*

F. S., a 26-year-old Negro gravida i, para 0, entered the hospital on April 27, 1952, in active labor at term. The blood pressure was 120/80, the urine negative for albumin, the blood counts within normal limits, serological test for syphilis negative, and there was nothing unusual in the patient's general condition, nor her labor. At 4 cm. dilatation she was given Demerol, 100 mg., and scopolamine, 1/150 grain. With complete dilatation she was delivered normally under cyclopropane anesthesia, assisted by a median episiotomy. During the induction of anesthesia a carpopedal spasm and a stiffening of the body were noted but disregarded because of the normal blood pressure.

Following the delivery and repair, the patient failed to regain consciousness although she did respond to tactile stimuli. As she was returned to bed the attendant noticed that periodically she waved her arms about and stiffened the lower extremities. The nurse left the room for a moment and when she returned she found the patient lying on the floor. There was no evidence of head injury, and when the patient was replaced in bed episodes of waving of the arms and stiffening of the legs became more frequent and pronounced. The blood pressure was 126/70, pulse 128, respirations 40. Sedation, intravenous fluids, and oxygen were immediately started. A note by the resident stated that convulsions did not involve the face, there was frothing at the mouth, but at no time was

a mouth gag necessary. Tonic convulsion of the arms recurred every few minutes, but there was no clonic component. These convulsions continued at irregular but frequent intervals for 5 days at which time they increased to the point where they were almost continuous. The condition seemed desperate.

Neurological findings showed definite and marked motor impairment of combined pyramidal and extrapyramidal origin with cogwheel rigidity which was very rapid in supination, elbow extension and flexion; Babinski and Chaddock signs were positive on the right.

Lumbar puncture showed a pressure of 230 mm. of water; the spinal fluid was clear and colorless.

A diagnosis was made of a diencephalic lesion, probably on a vascular basis.

On the sixth, seventh, and eighth days after the onset of the cerebral accident the blood pressure fluctuated between 144/108 and 188/130, then gradually diminished to normal levels by the time the patient was discharged from the hospital. At no time was there more than 20 mg. of albumin in the urine. She responded slowly to treatment which included ACTH, anticoagulants, tracheotomy, calcium gluconate intravenously, oxygen, and heavy sedation. She was discharged on May 28, 1952, one month after the cerebral vascular accident, with considerable residual motor damage, but able to care for herself.

In March, 1953, some 11 months after her episode, she was re-entered in our prenatal clinic because she was again pregnant, and her expected date of confinement was Oct. 18, 1953. At this time she was found to have made a remarkably complete recovery. Her prenatal course was uneventful; the highest blood pressure recording was 140/90 on one occasion. At no time was there any albumin reported in the urine; no edema of the lower extremities and no subjective symptoms were noted.

Her labor at term was of short duration. She was given Demerol, 100 mg., together with scopolamine, 1/150 grain, during the first stage of labor and nitrous oxide-oxygen anesthesia during the second and third stages. She was discharged with her baby on the fifth postpartum day in good condition.

CASE 4.—*Cerebral thrombophlebitis with complete recovery and instrumental delivery of a living child.*

M. P., a 27-year-old white gravida ii, para i, was admitted to the hospital on Oct. 21, 1951, because she had had a convulsion lasting 2 minutes during the previous evening and again that morning just before admission. Her last menstrual period was May 13, 1951, and the expected date of confinement was Feb. 9, 1952.

The past history disclosed a left nephrectomy in 1947, and in uneventful pregnancy and delivery at term, one year previously.

Initial examination showed a blood pressure of 125/76, pulse 80, respirations 20, and the abdomen enlarged by a tumor of pregnancy of approximately 5 months' gestation. The patient was lethargic, disoriented, and confused. Neurological findings disclosed that all of the cranial nerves were normal, the biceps and triceps reflexes were notably greater on the left, while the Chaddock sign was positive on the right.

Spinal puncture registered an opening pressure of 360 mm. of water, the fluid was clear and colorless, the cell count showed 2 erythrocytes. The serological test for syphilis was negative, the urine contained no albumin, and the blood counts and chemistry were within physiological limits.

A diagnosis of cerebral venous thrombophlebitis was made and the patient made a rapid and complete recovery under a regime of general supportive treatment.

On Feb. 8, 1952, she was readmitted to the hospital, at term, in active labor. She was given morphine sulfate, 1/6 grain, and scopolamine, 1/150 grain during the first stage of labor, and under cyclopropane anesthesia was delivered of a living child by forceps at the outlet.

She was discharged on the seventh postpartum day in good condition.

CASE 5.—*Cerebral thrombosis with recovery and instrumental delivery of a living child.*

F. W., a 30-year-old white gravida i, para 0, was admitted to the hospital on July 27, 1951. Since early morning she had noticed a progressive weakness of the hands which resulted in dropping many objects handled in the kitchen. The weakness became more pronounced and she fell to the floor; from there she made her way to the telephone where she called for assistance. Her last menstrual period had occurred on Oct. 25, 1950, and the expected date of confinement was Aug. 1, 1951.

Her past history was noncontributory except for an automobile accident at 18 years of age, in which she sustained a head injury and was hospitalized for 3 weeks, but recovery was said to be complete.

Physical examination was essentially negative except for an extreme drowsiness, a definite weakness and inactivity of the left side, which slowly progressed to complete hemiplegia within 24 hours. The blood pressure was 110/65, pulse 84, respirations 20. The uterus appeared to be near term and contained a fetus in the left occiput anterior position, with regular fetal heart tones and the presenting part engaged.

The serological test for syphilis was negative, the urine contained no albumin, and the blood counts were within physiological limits.

Lumbar puncture produced a clear, colorless fluid under pressure of 120 mm. of water.

A diagnosis of right cerebral thrombosis, probably in the brain stem, was made. The prognosis was equivocal, and we hoped for delay of delivery as long as possible. No anticoagulants could be used because of the imminence of labor.

Stellate blocks, in an attempt to dilate the cerebral vessels, were performed on two separate occasions, but produced little or no improvement. She responded slowly but steadily to general supportive management, gradually recovering her speech and motor activity.

On Aug. 18, 1951, 3 weeks after the cerebral episode, and 17 days after her expected date of confinement, she went into active labor. She was given Demerol, 100 mg., and scopolamine, $\frac{1}{150}$ grain, during the first stage of labor, and under cyclopropane she was delivered of a living child by forceps.

She made rapid improvement after delivery and left the hospital some 2 weeks later with a minimum of residual motor paralysis.

CASE 6.—*Cerebral thrombosis terminating in death and verified at autopsy.*

J. H., a 37-year-old Negro gravida ii, para i, entered the hospital on March 3, 1955, because her husband said she was stuporous and disoriented. Her last menstrual period had occurred on Jan. 1, 1955.

Her past history was noncontributory. She had had an uneventful pregnancy and labor 10 years before.

Upon admission her pulse was 66, temperature 98.6° F., respirations 24, blood pressure 126/84. The patient was lethargic, incoherent, disoriented, irrational, and showed impairment of memory for recent and remote events. Neurological findings showed the right pupil larger than the left and sluggish reaction of both; there was nystagmus on attempting to look in either direction. Motor paralysis of the fifth cranial nerve was present on the left side. There was no hemiplegia but some sensory impairment on the right side with ankle clonus on both right and left sides.

Lumbar puncture showed a clear fluid under 220 mm. water pressure.

The serological test for syphilis was negative. The urine contained no albumin and the blood counts were within physiological limits. Blood chemistry determinations, prothrombin time, and coagulation time were normal. The bleeding time was 2 minutes and the Lee-White coagulation time was 8 minutes.

A diagnosis of cerebral thrombosis of the left midbrain and pons (superior cerebellar artery) was made, and the prognosis for recovery was equivocal.

General supportive treatment was instituted, including anticoagulants (heparin and Dicumarol), but to little avail. The patient's condition continued to deteriorate rapidly, she lapsed into a profound coma, and died on March 8, 1955, four days after the onset of symptoms.

Findings at autopsy revealed obturator thrombosis of the basilar artery of the brain; marked encephalomalacia of the left cerebellar hemisphere, hypertrophy of the uterus, and products of early gestation therein.

Summary and Results

The literature on cerebral vascular accidents, both hemorrhage and thrombosis, occurring during pregnancy without eclampsia, has been briefly reviewed.

In a total of 8,036 patients delivered over a period of 5 years, we encountered 6 vascular accidents (approximately 1 per 1,400) complicating pregnancy without eclampsia. Of these, 2 were spontaneous subarachnoid hemorrhages and 4 were cerebral thromboses.

The time of occurrence of the cerebral hemorrhages was at 3½ and 6 months' gestation; that of thrombosis 6 weeks, 5 months, and 3 weeks prior to delivery, and one in the late second stage of labor.

It is interesting to note that in Case 3 (F. S.) of the cerebral thrombosis series, with an initial blood pressure of 126/90, hypertension fluctuating between 144/108 and 188/130, associated with mild albuminuria, developed on the sixth, seventh, and eighth days following the vascular accident.

I am fully aware of the unreliability of statistics in such a small series but the maternal mortality for the entire group of 6 cases of cerebral vascular accident was 16⅔ per cent, and for cerebral thrombosis, 25 per cent. The fetal mortality duplicated that of the maternal.

Each patient in the series was treated by so-called conservative management, both for the cerebrovascular lesion and the pregnancy.

No one can predict or foresee the long-term damage done to these patients so treated, but the results of our series herein reported seem to indicate that cerebral vascular accidents occurring during pregnancy, while admittedly extremely grave, are not entirely hopeless.

Of the 5 patients who recovered, 4 were able to continue to term without incident and the other who suffered the accident in the late second stage of labor became pregnant again soon afterward and continued to term and delivery again without incident.

References

1. Batson, O. V.: Ann. Surg. **112**: 138, 1940.
2. Bristowe, J. S.: Quoted by Dowie.[7]
3. Conley, J. W., and Rand, C. W.: A. M. A. Arch. Neurol. & Psychiat. **66**: 443, 1951.
4. de Carle, D. W.: West. J. Surg. **57**: 181, 1949.
5. Dereaux, M. M. J., et Dereaux, J. E.: Bull. et mém. Soc. méd. hôp. Paris, p. 303, March 11, 1955.
6. Descher, E. A., and Rowe, E. C.: Am. J. Surg. **85**: 561, 1953.
7. Dowie, R.: Brit. M. J. **2**: 547, 1952.
8. Egas Moniz: Rev. d'oto-neuro-opht. **11**: 746, 1933.
9. Eller, N. C.: Am. J. Obst. & Gynec. **52**: 488, 1946.
10. Feldman, R. L., Gross, S. W., and Wimpfheimer, S.: Am. J. Obst. & Gynec. **70**: 289, 1955.
11. Gerin-Rose: 1859. Quoted by Weigle.[30]
12. Jones: Quoted by Wechsler and Gross.[29]

13. Kendall, D.: Brain **71**: 386, 1948.
14. King, A. G.: J. A. M. A. **100**: 15, 1933.
15. Lazard, E. M.: Philadelphia M. J. **4**: 1901.
16. Mackenzie, S. M.: Brit. M. J. **1**: 824, 1933.
17. Masten, M. G.: Wisconsin M. J. **34**: 168, 1935.
18. McNairn, J.: J. Obst. & Gynaec. Brit. Emp. **55**: 630, 1948.
19. Quick, A. J.: Surg., Gynec. & Obst. **91**: 296, 1950.
20. Richardson, J. C., and Hyland, H. H.: Medicine **20**: 1, 1941.
21. Rhoades, E. E.: AM. J. OBST. & GYNEC. **54**: 533, 1947.
22. Schreiber, F.: Harper Hosp. Bull. **3**: 68, 1945.
23. Schwartz, J. J.: AM. J. OBST. & GYNEC. **62**: 539, 1951.
24. Slemons, J. M.: Johns Hopkins Hosp. Bull. **18**: 448, 1907.
25. Stefanini, Mario: J. Mt. Sinai Hosp. **19**: 619, 1953.
26. Strauss, I., and Tarachow, S.: Arch. Neurol. & Psychiat. **38**: 239, 1937.
27. Ullery, J. C.: AM. J. OBST. & GYNEC. **68**: 1243, 1954.
28. Walton, J. N.: Brit. M. J. **1**: 869, 1953.
29. Wechsler, I. S., and Gross, S. W.: J. A. M. A. **136**: 517, 1948.
30. Weigle, E. H.: AM. J. OBST. & GYNEC. **69**: 888, 1955.
31. Wilson, S. A. K., and Bruce, A. N.: Neurology, Baltimore, 1955, Williams & Wilkins Company, vol. 3.

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Discussion

DR. ROLAND P. MACKAY.—This paper draws attention to the problem of the maternal neurological catastrophe occurring at or near labor. These castastrophes are not different in pregnant women from those seen in others except for certain special aspects. Of course, the complication of a neurological emergency by the presence of pregnancy is a very great one. In the later stages of pregnancy the clotting activity of the mother's blood is increased with greater likelihood of thrombosis. It is very difficult to discuss cerebral vascular catastrophes as a whole group because, as Dr. Finola has shown, there are many varieties. These same conditions occur in young people, in old people, in males and females, and they consist of hemorrhages, thromboses, intracerebral, subdural, and subarachnoid hemorrhages; and one must differentiate these types of disorders to make a careful plan of management.

The first differentiation of cases is into hemorrhage and thrombosis. Hemorrhages may be intracerebral and these are indeed difficult to distinguish from intracerebral thromboses. One reads a lot in textbooks on methods of distinguishing them but at the bedside the differentiation is difficult. That means further hesitation in the use of anticoagulants, because anticoagulants are contraindicated in hemorrhagic states. If there is massive intracerebral hemorrhage, the intracerebral hematoma may be removed surgically if it is properly diagnosed and localized. I will not go into the diagnosis except to say that in hemorrhage there is a sudden onset of coma followed by increasing intracranial pressure and progressive neurological deficit. Subarachnoid hemorrhage, which occurred in 2 of Dr. Finola's cases, is seen to be highly important from the fact that it accounts for 4.7 per cent of all sudden nonaccidental deaths; that is, almost one out of 20 people who die suddenly and are not killed by accident die of subarachnoid hemorrhage. It constitutes 25 per cent of all sudden deaths from neurological causes. These figures were taken from the New York City vital statistics for the year 1950.

The etiology of subarachnoid hemorrhage is for all practical purposes congenital aneurysm, an anomaly occurring equally in men and women and leading to hemorrhage, especially in young adults, when sufficient pressure is present to rupture the aneurysm. The diagnosis is usually easy because such patients present a typical clinical picture of sudden onset of meningitis without fever. One sees a stiff neck and positive Kernig and Brudzinski signs. The final diagnosis depends on spinal puncture.

The prognosis of subarachnoid hemorrhage is intriguing. Statistics on all people with subarachnoid hemorrhage show that 50 per cent die in the first 8 weeks following the first attack; the mortality rates in the pregnant and nonpregnant are about the same.

The therapy of such conditions in pregnant women should be conservative, as in the cases which Dr. Finola described. It ought to be conservative in all people for quite a while, and especially in pregnant patients. Operative treatment of ruptured congenital aneurysm with subarachnoid hemorrhage is designed to prevent similar attacks in the future, and not to treat the attack which has already occurred. These patients should be left alone, recumbent or semirecumbent. If rupture occurs at the time of delivery, you will have to use your own best clinical judgment as to the proper procedure. I have no rules to give you.

As to thrombosis, one recalls that coagulability of the blood is increased in the later stages of pregnancy, a fact predisposing to thrombosis. One should mention venous thrombosis as well as arterial, because it is perhaps especially apt to occur in the pregnant woman, either before or after delivery. These may be simple venous thromboses or may result from thrombophlebitis, with or without heart disease or infection elsewhere in the body. Management must be conservative in these cases, too. Anticoagulants are certainly contraindicated shortly before labor. I do not know how soon after delivery one may safely use them. It depends on how soon coagulability of the blood returns to a normal level. Antibiotics should be used if thrombosis is due to phlebitis. One should avoid the use of the commonly acceptable vasodilators such as Priscoline or Dibenamine. These dilate noncerebral blood vessels but not those in the brain, resulting in unchanged or diminished cerebral blood flow. Cerebral blood flow may be increased with papaverine given in doses of 0.1 Gm. orally three or four times daily. A better method is to give inhalations of 5 per cent carbon dioxide in 95 per cent oxygen through a Boothby mask, which can be done easily at the bedside for, say, 10 minutes in each hour.

PEPTIC ULCER IN PREGNANCY

A Report of 3 Cases

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PEPTIC ulcers are less common in women than men and are rare in pregnancy. The symptoms due to ulcers usually improve during pregnancy.[2, 5]

Sandweiss and associates[26] found only one maternal death due to a complication of peptic ulcer in all maternal admissions of five large Detroit hospitals in 10 years. This study encompassed 70,000 patients. These same authors studied 46 women with ulcers, 25 of whom became pregnant. All but one of these patients noted relief of ulcer symptoms during the pregnancy. Durst,[11] reporting one death as a result of a complication of peptic ulcer in pregnancy, noted 6 cases of peptic ulcer in 149,491 patients who were admitted for delivery during 9 years at Milwaukee Hospitals. Hooker[14] studied all the maternal deaths at New York City Hospitals and found only one case of gastric ulcer during the years 1930 to 1933. Clark[10] reported on 118 women who had 344 pregnancies, over 90 per cent of whom noted remission of their ulcer symptoms. In no instance were there any complications of ulcer such as hemorrhage or perforation. Most patients welcomed pregnancy as a relief from their pain.

Complications of peptic ulcer during pregnancy necessitating surgery are rare. Mussey,[21] in a 10 year period at the Mayo Clinic, noted no case of complication of peptic ulcer which necessitated operation.

Case reports of deaths due to complications of peptic ulcer in pregnancy have appeared in the literature. Most complications arise in the third trimester and many are related to toxemia.[3, 7-9, 12, 13, 15-18, 20, 23, 24]

The following case is an example of an ulcer apparently occurring during the last trimester of two pregnancies, which finally penetrated the posterior duodenum and produced massive gastrointestinal hemorrhage necessitating a subtotal gastric resection.

CASE 1.—A 26-year-old white woman was admitted to Miami Valley Hospital, Dayton, Ohio, by ambulance Dec. 19, 1955, complaining of hematemesis and weakness. In June of 1954, when she was in the seventh month of her first pregnancy, she noted the onset of burning epigastric pain which was relieved by milk. This pain persisted and went through to the back, and soon it was no longer relieved by milk or alkali. The pain became intense and radiated around the costal cage. It was assumed that she had muscular pain due to the pregnancy. On Aug. 17, 1954, she was delivered of a normal infant. The pain gradually subsided and in three weeks she was well.

In October, 1955, approximately one year later, she was 6 months pregnant and again noted the onset of back pain radiating around the costal cage, which became more severe and finally was accompanied by nausea and vomiting. On Dec. 11, 1955, after a premature separation of the placenta, she was delivered of a 4½ pound stillborn infant. She had never shown any hypertension and all urinalyses were negative for albumin.

Eight days later, while traveling by plane from the East to this city, she vomited a large quantity of partially digested blood.

Examination on admission showed a slight, pale woman, 5 feet, 1 inch tall, weighing 90 pounds, in acute distress. She was complaining of acute thirst. The blood pressure was 110/80, and pulse rate 110. The mucous membranes were pale. On admission the erythrocyte count was 2.9 million, hemoglobin 8.8 Gm., and hematocrit 27 volumes per cent. The total blood volume, determined by the use of radioactive serum albumin, showed a red-cell deficit of over 500 c.c.

She was given 500 c.c. of whole blood, which improved her condition. On Dec. 22, 1955, the third hospital day, an x-ray examintation of the upper gastrointestinal tract showed marked edema of the duodenal mucosal folds and marked spasticity, indicating an active duodenal ulcer. She bled again that morning and was given 1,500 c.c. of whole blood, but continued to bleed and early in the morning of Dec. 23, 1955, she was in shock with a blood pressure of 80/0 and a pulse rate of 132. A subtotal gastric resection was performed on December 23, and a large posterior penetrating duodenal ulcer with an actively bleeding vessel in the base was found. The ulcer had eroded most of the posterior wall of the second part of the duodenum.

A second case of an active duodenal ulcer complicating pregnancy has been encountered in our practice. This patient noted increasing symptoms with pregnancy which prompted her to present herself for examination. She was referred to Dr. Everett W. Shank for final diagnosis and therapy.*

CASE 2.—The patient, aged 23 years, para ii, was first seen in January, 1945, at which time she was in the first trimester of pregnancy, complaining of epigastric distress. She noted burning epigastric pain which occurred around two or three hours after eating. This pain was relieved by milk. She had noted some distress before pregnancy, but felt it had increased since she became pregnant. An x-ray examination taken in January, 1945, showed an active duodenal ulcer. She was treated by modified Sippy regime and responded well. She had no hemorrhage.

This case is presented to show that the epigastric distress of early pregnancy may have a demonstrable organic basis. This patient was managed successfully with a medical regime. A re-examination by x-ray of the upper gastrointestinal tract in 1946 showed no evidence of an ulcer.

CASE 3.†—This 24-year-old woman was followed through two pregnancies. During the first of these she had no gastrointestinal symptoms. She was first seen in 1951, at which time she had toxemia of pregnancy. She was later delivered by cesarean section on November 2 of a viable baby.

She was again seen on Jan. 9, 1954, at which time she was 8½ months pregnant, complaining of lightheadedness, tarry stools, and vomiting of coffee-ground material. She was admitted to the hospital with a presumptive diagnosis of bleeding peptic ulcer or bleeding esophageal varices. She was treated with blood transfusion, but on Jan. 17, 1954, she was delivered of a stillborn infant. X-ray studies of the upper gastrointestinal tract, done following delivery, showed spasm of the duodenum consistent with a duodenal ulcer. She was treated with antacids and responded well.

She was seen once again in April, 1956, at which time she was again pregnant. She had no complaints with this pregnancy, and examination showed no abnormalities.

Comment

Although peptic ulcers in pregnancy are rare, the influence of hormones upon peptic ulceration has been the subject of many investigative works.

*This case is presented by permission of Dr. Shank.
†Presented through the courtesy of Dr. Roger E. Fox of Media, Pa.

Sandweiss[28] noted the healing and prevention of ulcers in Mann Williamson prepared dogs* by the administration of anterior pituitary hormone. The authors were led to this work by having noted the rarity of ulcers in pregnancy.

They[27] treated a few patients with this substance and noted some improvement. They also noted that in young children who have a small amount of circulating sex hormone the incidence of ulcers is about the same in male and female. In fact, in younger children who have the least circulating sex hormone, the incidence of peptic ulcer was greater in females[25] This study seems to point to the protective factor of the female sex hormone. Abrahamson[1] treated a group of male ulcer patients with estrogen and noted a slight improvement. He did not recommend the use of this therapy, however.

The anterior pituitary extract (Pitressin) has been used to produce ulcers in experimental animals by the University of Illinois group.[6, 22] Metz[19] has also produced in rabbits a gastric lesion characteristic of an ulcer by injecting large doses of posterior pituitary extract. He had, however, treated ulcer patients with smaller doses of this extract with apparently good results.

Summary

Three cases of active peptic ulcer occurring in pregnancy are presented. Two of these cases were complicated by hemorrhage.

References

1. Abrahamson, R. H., Church, R., and Hinton, J. W.: Am J. M. Sc. **204**: 809, 1942.
2. Adair, F. L., and Stieglitz, E. J.: Obstetric Medicine, Philadelphia, 1934, Lea & Febiger, pp. 472-478.
3. Anderson, G. W.: Am. J. Obst. & Gynec. **43**: 883, 1942.
4. Artz, Franz: Am. J. Obst. & Gynec. **20**: 382, 1930.
5. Backus, H. L.: Gastroenterology, ed. 2, Philadelphia, 1946, W. B. Saunders Company, vol. 1, p. 340.
6. Berg, Max: Am. J. Digest. Dis. **7**: 78, 1940.
7. Bernstine, J. B., and Friedman, M. H. F.: Am. J. Obst. & Gynec. **56**: 973, 1948.
8. Bralow, S. P., Scheinberg, S., and Necheles, H.: Am. J. Digest. Dis. **15**: 137, 1948.
9. Carangelo, J., and Efstation, T. D.: Am. J. Obst. & Gynec. **56**: 191, 1948.
10. Clark, D. H.: Brit. M. J. **1**: 1254, 1953.
11. Durst, J. B., and Klieger, J. A.: Am. J. Obst. & Gynec. **70**: 448, 1955.
12. Greely, A. V., and Slubenbord, W. D.: Am. J. Obst. & Gynec. **42**: 154, 1941.
13. Hahn, G. A.: Am. J. Obst. & Gynec. **63**: 222, 1952.
14. Hooker, R. S.: Maternal Mortality in New York City, New York, 1933, The Commonwealth Fund, p. 233.
15. Humpstone: Am. J. Obst. **73**: 1114, 1916.
16. James, D. W.: Brit. M. J. **2**: 74, 1948.
17. Johnston, J. L.: Am. J. Obst. & Gynec. **2**: 290, 1953.
18. LeWinn, E. B.: Am. J. Obst. & Gynec. **54**: 114, 1947.
19. Metz, M. H.: Texas J. Med. **34**: 295, 1938.
20. Mulsow, F. W., and Brown, W. E.: Am. J. Obst. & Gynec. **31**: 1041, 1936.
21. Mussey, R. D.: Proc. Staff Meet. Mayo Clin. **2**: 156, 1927.
22. Nedzel, A. J.: Arch. Path. **26**: 988, 1938.
23. O'Connell, W. T.: Am. J. Obst. & Gynec. **70**: 416, 1955.
24. Rider, J. A., Kisner, J. B., and Palmer, W. L.: Gastroenterology **24**: 357, 1953.
25. Saltzstein, H. C., Farbman, A. A., and Sandweiss, D. J.: Endocrinology **27**: 400, 1940.
26. Sandweiss, D. J., Podolsky, H. M., Saltzstein, H. C., and Farbman, A. A.: Am. J. Obst. & Gynec. **45**: 131, 1943.
27. Sandweiss, D. J., Saltzstein, H. C., and Farbman, A. A.: Am. J. Digest. Dis. **6**: 6, 1939.
28. Sandweiss, D. J., Saltzstein, H. C., and Farbman, A. A.: Am. J. Digest. Dis. **5**: 24, 1938.

*Division of the stomach at the pylorus, closure of the distal end of pylorus, anastomosis of the proximal pyloric end to the side of the lower jejunum.

VOMITING DURING PREGNANCY DUE TO MIDGUT VOLVULUS WITH DUODENAL OBSTRUCTION*

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SYMPTOMS produced by the majority of the congenital malformations of the gastrointestinal tract tend to appear during the early weeks or months of life.[6] This also is true of most of the anomalies of intestinal rotation and fixation. Over one half of these patients may be expected to experience symptoms during the first month of life.

In order to understand these abnormalities more fully, it is desirable to have an insight into their potential embryogenesis. During the period from the sixth to the tenth week of embryonic life, a segment of the midgut passes temporarily into the base of the umbilical cord. It has been suggested that this results at this time from a more rapid growth of the intestinal tract than of the celomic cavity. At approximately the tenth week, the extracelomic intestine begins to return to the peritoneal cavity. In doing so, the midgut rotates in a counterclockwise manner so that the cecum and terminal ileum come to lie in the right lower quadrant of the abdomen. The mesocolon of the ascending and descending colon becomes fused with the peritoneum of the posterior abdominal wall at the completion of this rotation, thus anchoring the mesentery.

Disturbances in this process of rotation and fixation may create several different types of malformation. The mesentery may not be attached to the posterior abdominal wall, a condition predisposing to the occurrence of a midgut volvulus. In some instances the pressure of the superior mesenteric vessels, supporting an otherwise unsupported small intestine, may produce obstruction at the level of the third portion of the duodenum. The occurrence of some degree of volvulus may tighten this vascular "cord" lying over the duodenum and further aggravate the obstruction. The greatest hazard of midgut volvulus, however, lies in occlusion of the vessels from the torsion process with resulting infarction of the midgut. Gangrene, perforation, peritonitis and death may occur in a short period of time. In addition, the cecum may not be completely rotated and may be so placed that it causes duodenal obstruction either by direct pressure or indirectly by bands. It is of interest that Gross[3] has reported that approximately one half of the patients at the Children's Hospital in Boston, who have been operated upon because of duodenal obstruction from an incompletely rotated cecum, have also been found to have a volvulus of the midgut.

*Aided in part by a grant from the James Whitcomb Riley Memorial Association.

In some cases, the cecum may be completely rotated but unattached. This exceedingly mobile condition of both the cecum and the right colon may predispose to volvulus of these structures. This tends to occur more often in adults, in contrast to the difficulties produced by the other abnormalities of intestinal rotation and fixation. Although this problem has been discussed in greater detail elsewhere,[5] it is of interest to note that volvulus of the cecum and right colon has been reported during pregnancy and labor. Finally, one must regard those paraduodenal and paracecal recesses into which herniation of the small intestine may take place as defects of intestinal rotation and fixation.

It has seemed desirable to report a rather unusual case of duodenal obstruction during pregnancy in an 18-year-old girl. The obstruction was produced during the third month of pregnancy by a midgut volvulus, secondary to a nonattached dorsal mesentery, with pressure on the third portion of the duodenum from the torsion of the superior mesenteric vessels.

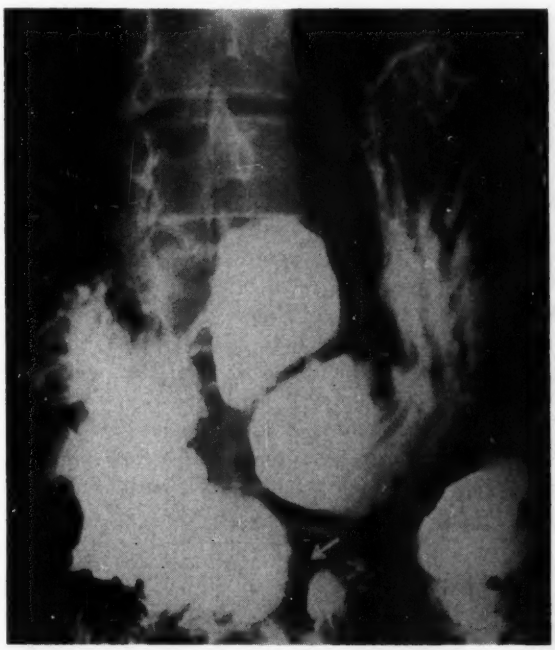

Fig. 1.—Roentgenogram taken following the administration of barium by mouth, showing distention of the first and second parts of the duodenum with an obstruction at the level of the third part of the duodenum (arrow). Barium enema had been given prior to this examination.

Case Report

The patient, an 18-year-old, white, married woman, was admitted to the Ball Memorial Hospital on Sept. 8, 1953, because of nausea and vomiting of two weeks' duration. She was known to be three months pregnant. She was dehydrated and had lost 14 pounds of weight in the two weeks prior to her admission to the hospital. The vomiting seemed to occur approximately one-half hour after eating and the vomitus contained bile. This was the patient's first pregnancy. There was no family history of congenital malformation.

The patient had experienced recurrent episodes of crampy abdominal pain with nausea and vomiting since childhood. Although she had been studied during hospital

admissions at 11 and 12 years of age, the cause of her difficulties had never been satisfactorily explained. None of her previous attacks had equaled the present one in severity. She had more or less come to accept this type of trouble, associated with her eating, as a part of her way of life.

On physical examination, the patient was found to be a slim, somewhat emaciated appearing young woman who weighed 96 pounds. The blood pressure was normal and the other findings were all essentially within normal limits. The abdomen was soft. No tenderness, masses, nor distention could be found. The bowel sounds appeared to be normal at the time of examination. The findings on examination of the urine were not remarkable. The hemoglobin was 17.5 Gm. and the red blood count 5.5 million. The leukocyte count was 14,300 with 87 per cent neutrophils and 18 per cent band forms. A portion of this change in the blood picture was regarded as secondary to the patient's state of dehydration.

On roentgen examination of the upper gastrointestinal tract with barium, considerable distention of the first and second parts of the duodenum were visualized. There appeared to be a partial obstruction of the third portion of the duodenum with marked narrowing of the lumen at this level (Fig. 1). The cecum was observed to be somewhat higher on the right side than usual during the barium enema examination. The findings on this examination were otherwise within normal limits.

The patient was taken to the operating room at the completion of the diagnostic studies and following the replacement of lost fluids and electrolytes. The peritoneal cavity was opened through an upper right rectus muscle retracting incision. When the peritoneal cavity was entered, a midgut volvulus was found with approximately one complete turn on the superior mesenteric vessels. The dorsal mesentery was not attached to the posterior abdominal wall and the small intestine was suspended from the superior mesenteric vessels. The volvulus had not produced ischemia of the intestines but rather had led to duodenal obstruction in the third portion from the pressure produced from the overlying superior mesenteric vessels which had become twisted. The cecum was in the right lower quadrant but was quite mobile. Numerous ancient-appearing adhesions were found in the mesentery. These most likely had been formed in the wake of some of the previous episodes of abdominal discomfort. It was quite apparent that a duodenojejunostomy was the procedure of choice in this situation. Following partial derotation of the midgut volvulus, a duodenojejunostomy was carried out in two layers. A continuous No. 3-0 chromic catgut suture was used for the inner layer and interrupted Halsted mattress sutures of No. 3-0 silk were employed for the outer layer. An ample lumen was obtained. The incision was closed in layers with interrupted sutures of fine silk and the patient was returned to the ward in good condition.

Her postoperative course was completely uneventful. There was no vomiting or evidence of duodenal obstruction and her recovery was prompt. She was discharged from the hospital seven days following operation. There was no recurrence of the symptoms of abdominal pain or vomiting throughout the remainder of her pregnancy and she gave birth without difficulty to a full-term normal male infant on April 15, 1954. In the 20 months since her operation, she has remained completely free of the symptoms which had plagued her so frequently and for so many years.

Comment

This case is of interest because of the long history of chronic and recurrent difficulty with nausea, vomiting, and abdominal pain prior to the rather sudden and considerably more virulent exacerbation of symptoms during the early months of the patient's first pregnancy at 18 years of age. The midgut volvulus had produced sufficient twisting and tightening of the superior mesenteric vessels over the third portion of the duodenum to produce an obstruction

at this level without significantly compromising the blood flow through these vessels. The old mesenteric adhesions which were found suggested that the previous symptoms were most likely on a similar basis. Following the duodenojejunostomy, the patient experienced marked and dramatic relief of her symptoms for the remainder of her pregnancy and during the months since the delivery of her child.

The occurrence of intestinal obstruction due to volvulus during pregnancy is quite rare. Although an occasional case has been reported in which the volvulus involved the cecum, the sigmoid colon, or an isolated loop of small intestine,[1, 4, 5] I have been able to discover only one other case of midgut volvulus during pregnancy. This case was reported by Donald[2] in 1927. The patient was a 27-year-old woman who was 5 months pregnant. She had suffered from a similar, but milder, episode of colicky abdominal pain with vomiting at 25 years of age. At operation, a midgut volvulus was found with 2.5 turns in a clockwise direction. The small intestine was quite distended. There was marked impairment of its blood supply with early gangrene. The patient was managed by derotation of the volvulus and cecostomy. She died four hours postoperatively.

It must be remembered that the symptoms of intestinal obstruction, such as nausea, vomiting, and crampy abdominal pain, may resemble the symptoms of other complications of pregnancy. This may lead to confusion and an undue delay in establishing the diagnosis and the condition of the patient may have deteriorated materially in the interim. The value of roentgen study of the abdomen and of careful abdominal auscultation in facilitating early diagnosis cannot be too strongly emphasized.

The ages at which symptoms tend to occur with these malformations of intestinal rotation and fixation are well illustrated by the findings of Gross.[3] Eighty-seven of his 156 patients were in the first month of life, 40 were between the first and twelfth months, and 29 were between one and 15 years of age. It is clear that the occurrence of midgut volvulus in adult life is quite rare indeed. The role of pregnancy in precipitating an acute episode with exacerbation of symptoms is unknown.

Summary

An interesting case of severe vomiting with dehydration and weight loss due to midgut volvulus with duodenal obstruction during pregnancy is reported. The patient was an 18-year-old primipara in the third month of pregnancy. She had experienced symptoms which were similar, but much less severe, for many years. The obstruction occurred at the level of the third portion of the duodenum and was produced by the torsion and tightening of the overlying superior mesenteric vessels. These vessels were the only support for an otherwise unattached small intestine. Complete and continuing relief of the patient's symptoms was achieved by operative by-pass of the area of obstruction

by means of a duodenojejunostomy. The episode of obstruction and its operative management did not influence the normal course and termination of the pregnancy. The importance of an awareness of the possible occurrence of intestinal volvulus during pregnancy is emphasized.

References

1. Barone, C. J., Power, H. A., and Kuhn, C. L.: Am. J. Obst. & Gynec. 41: 890, 1941.
2. Donald, C.: Brit. J. Surg. 15: 269, 1927.
3. Gross, R. E.: The Surgery of Infancy and Childhood, Philadelphia, 1953, W. B. Saunders Company.
4. Kornfield, G., and Daichman, I.: Am. J. Obst. & Gynec. 27: 768, 1934.
5. Moore, T. C.: J. Indiana M. A. 47: 237, 1954.
6. Moore, T. C., and Harris, E. J.: J. Indiana M. A. 47: 1390, 1954.

THE USE OF 6-MERCAPTOPURINE IN TREATMENT OF ACUTE LEUKEMIA IN LATE PREGNANCY

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MORE than 115 cases of leukemia associated with pregnancy have been reported in the literature. This case is presented because 6-mercaptopurine was used in the management of this disease in late pregnancy, with a result suggestive that this drug should be added to our armamentarium for treatment of acute leukemia complicating late pregnancy without apparent ill effects on the fetus. Its efficacy in acute leukemia has been previously reported by Dameshek[1] and Burchenal and associates.[2]

Case Report

Mrs. L. R., a 23-year-old white woman, gravida ii, para ii, whose last menstrual period was April 17, 1955, was admitted to the hospital on Aug. 8, 1955, with severe anemia (hemoglobin 4 Gm., hematocrit 15 volumes per cent) and a chief complaint of "dizziness and giddy feeling for one and a half months."

Shortly after her admission, a bone marrow biopsy was performed and the diagnosis of acute myelocytic leukemia was made. During her month's stay, she received 8 pints of fresh whole blood, cortisone, 25 mg. four times a day, low-sodium diet, potassium supplement, vitamins, and iron medication. On discharge in late August her hemogram showed hemoglobin 10 Gm., hematocrit 29 volumes per cent, and a white blood count of 10,500. A differential count was not recorded at this time.

From August until November she was admitted only twice for blood transfusions and received a total of 8 more pints of fresh whole blood. On October 8, at 26 weeks' gestation, while the cortisone was continued, 6-mercaptopurine (25 mg. orally four times daily) was started, with the hope of obtaining a temporary remission. In November she was readmitted and was transfused with 4 pints of fresh whole blood. On Nov. 28, 1955, a low platelet count of 36,000 per cubic millimeter (Fonio method) was discovered, and the 6-mercaptopurine was discontinued. She was continued on cortisone, 25 mg. four times daily, low-sodium diet, potassium supplement, vitamins, and blood transfusions. On December 10, after 5 more transfusions of fresh whole blood the platelet count rose to 90,000 per cubic millimeter.

The patient did well until two weeks prior to delivery, when she developed complications of hydronephrosis, paresthesias in both legs, and paraplegia in a period of 72 hours. Because of the rapid deterioration of her condition labor was medically induced and she was delivered on Jan. 15, 1956, at 39 weeks' gestation, of a living 7 pound, 14 ounce baby girl, whose hemoglobin was 18 Gm. and hematocrit 63 volumes per cent. The infant's blood count and differential were entirely normal.

The mother's condition continued to deteriorate rapidly after the child's birth and she died at 11:48 P.M. on Jan. 22, 1956. Autopsy revealed the classical findings of acute myelocytic leukemia. The patient at the time of death had received a total of 50 pints of fresh whole blood, most of which was given in the last two months of her life.

Comment

This case demonstrated the use of 6-mercaptopurine in acute myelocytic leukemia late in pregnancy without any recognizable harmful effects on the fetus. It is difficult to say from this one case whether the 6-mercaptopurine had any significant effect on the disease or whether the cortisone or the great number of transfusions was the major factor.

References

1. Dameshek, W.: Ann. New York Acad. Sc. 60: 447, 1954.
2. Burchenal, J. H., et al.: Blood 8: 965, 1953.

GAUCHER'S DISEASE IN PREGNANCY*

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GAUCHER'S disease is a rare congenital and familial disorder of the intracellular lipoid metabolism. Abnormal storage of large amounts of cerebrosides takes place in the reticuloendothelial cells. The etiology of the disease is still unknown. It nearly always affects white people, especially Jews, and men and women equally. Other metabolic diseases, such as diabetes mellitus, are more common in patients with Gaucher's disease and their families.

The Gaucher cell is most commonly found in the liver, spleen, visceral lymph nodes, and bone marrow. Whitish collections of these cells may be seen grossly in affected tissues, accompanied by hemosiderosis. In the most common type of the disease the first sign is splenomegaly, averaging up to ten to fourteen times normal size. Fever is often present. Skin and scleral pigmentation are noted early and are progressive. Hepatomegaly occurs later and terminally there may be hepatic cirrhosis. The osseous type of the disease with spontaneous fractures is less common. The acute neurological type is seen only in infants and is always fatal. Blood findings in the usual type include leukopenia early, anemia late, latent jaundice from hemolysis, and decreased platelets.

The diagnosis is generally made by bone marrow puncture (Fig. 1). X-ray findings occur late and infrequently. Differential diagnosis is from other reticuloendothelial disorders, other causes of chronic splenomegaly, tumors and cysts, chronic splenic vein thrombosis, and Banti's syndrome.

No specific therapy for the disease is as yet known. Symptomatic treatment, for example, of anemia, is indicated. Splenectomy may be indicated in some instances, especially with hemorrhage, where it often results in symptomatic improvement, and also in cases where the spleen represents a hazard simply because of its size.

In the more chronic forms death generally occurs from intercurrent infections. The course is protracted, however, and the outlook generally is good. Widespread hemorrhagic changes may occur terminally due to decrease in platelets.

In a recent review of the available material on Gaucher's disease in pregnancy, we were able to find only 15 patients who had 35 pregnancies and 29 term deliveries. Sterility and repeated abortions are common, as is postpartum

*Presented at a meeting of the Chicago Gynecological Society, Feb. 15, 1957.

hemorrhage. Hence, aside from statements on the mechanical effect of splenomegaly, most information on the role of Gaucher's disease in pregnancy is largely theoretical or presumptive. Childbearing does not of itself cause maternal damage; therefore, despite the known increase in fetal and maternal hazards, in general, interruption of the pregnancy is not indicated. For medical reasons, splenectomy may occasionally be necessary, but the theoretical hazards of rupture or obstruction due to progressive splenomegaly in pregnancy do not justify it. There is at present no clear-cut evidence for hereditary transmission of Gaucher's disease to the offspring.

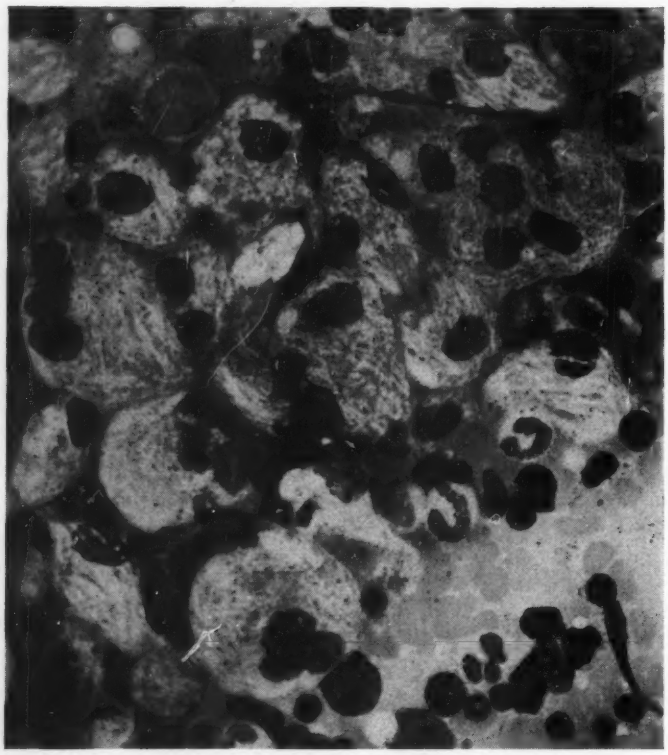

Fig. 1.—Gaucher cells from sternal puncture.

Case Report

Mrs. H. T. was a 32-year-old gravida iii, para ii, the wife of a physician. She was first seen on May 10, 1953, with a history of Gaucher's disease known since 1947, and amenorrhea of 7 weeks' duration. Her husband sought an opinion on the advisability of therapeutic abortion. She had always shown a tendency to develop ecchymoses, and a diagnosis of Gaucher's disease had been made in 1947 during her second pregnancy. Her family history was negative for Gaucher's disease or other metabolic disorders.

In February, 1947, in a U.S. Army Hospital at Frankfurt, Germany, she was delivered of a 7½ pound boy after an uneventful pregnancy and labor. The puerperium was complicated by a perineal hematoma. In February, 1948, in a Chicago hospital, she was delivered of a 7 pound, 9 ounce boy after an uneventful pregnancy and labor. The puerperium was uneventful.

On her first visit, physical examination revealed a uterus proportionate in size to the period of amenorrhea, a spleen enlarged to the umbilicus, and a liver palpable 2 fingerbreadths below the costal margin. Blood studies showed hemoglobin 13.9 Gm. (90 per cent), hematocrit 42 per cent, erythrocyte count 5.75 million, leukocyte count 7,700, platelets 644,000, a normal differential count, icterus index 15 units, reticulocyte count 4.4 per cent, sedimentation rate uncorrected 26 mm. per hour, mean corpuscular volume 73 cm., and mean corpuscular hemoglobin concentration 33 per cent (Table I).

TABLE I. BLOOD FINDINGS

DATE	TIME OF PREGNANCY OR PUERPERIUM (WEEKS)	ERYTHROCYTE COUNT (MILLIONS)	HEMOGLOBIN GM./100	LEUKOCYTE COUNT	PLATELETS	DIFFERENTIAL COUNT
5/10/53	7 pregnant	5.75	13.9	7,700	644,000	Normal
1/ 5/54	1 post partum	3.47	11.8	4,650	47,000	Normal
2/25/54	8 post partum	4.50	17.0	6,600	Adequate	Normal
1/ 6/55	14 pregnant	4.30	14.7	5,200	Adequate	Normal
7/ 9/55	1 post partum	3.79	12.6	--	Adequate	Normal
4/11/56	40 post partum	4.51	14.0	6,600	112,000	Normal

After consultation with the hematologist, Dr. Louis R. Limarzi, it was decided that there was no contraindication to continuation of the pregnancy, which was uneventful.

She entered the hospital at term in early labor. Physical examination showed a normal term pregnancy, *a spleen enlarged to the iliac crest,* and a *liver palpable 4 fingerbreadths below the costal margin.* On Jan. 1, 1954, she was delivered of an 8 pound, 12¾ ounce boy after a 7 hour labor terminated by outlet forceps and episiotomy. The puerperium was uneventful. Blood findings on the fourth postpartum day were: hemoglobin 11.8 Gm. (90 per cent), erythrocyte count 3.47 million, leukocyte count 4,650, differential count normal, platelets 47,000. Blood studies on the baby on the sixth day of life showed hemoglobin 18.7 Gm. (120 per cent), erythrocyte count 5.44 million, leukocyte count 5,500, differential count normal, platelets 83,000.

At the 6 weeks postpartum examination on Feb. 25, 1954, the uterus was well involuted and in good position, the *spleen was palpable 2 fingerbreadths above the iliac spine,* and the *liver was 3 fingerbreadths below the costal margin.* Laboratory examination of the blood 4 months post partum showed hemoglobin 17 Gm. (111 per cent), erythrocyte count 4.50 million, leukocyte count 6,600, differential count normal, and platelets adequate.

TABLE II. EXAMINATION OF LIVER AND SPLEEN

DATE	TIME OF PREGNANCY OR PUERPERIUM (WEEKS)	SPLEEN	LIVER
5/10/53	7 pregnant	Enlarged to umbilicus	2 fingerbreadths below costal margin
12/31/53	In labor	Enlarged to iliac crest	4 fingerbreadths below costal margin
2/25/54	8 post partum	2 fingerbreadths above iliac spine	3 fingerbreadths below costal margin
12/ 2/54	10 pregnant	Enlarged to umbilicus	2 fingerbreadths below costal margin
7/ 5/55	In labor	Enlarged to iliac crest	3 fingerbreadths below costal margin
8/18/55	7 post partum	Enlarged to umbilicus	3 fingerbreadths below costal margin
4/11/56	40 post partum	Enlarged to umbilicus	2 fingerbreadths below costal margin

On Dec. 2, 1954, the patient again presented herself pregnant, this time 9½ weeks since the last menstrual period. Despite some history of spotting and scanty vaginal bleeding during the preceding 2 weeks, the uterus was enlarged commensurately with the period of amenorrhea. The *spleen was then enlarged to the level of the umbilicus, the liver was palpable*

2 fingerbreadths below the costal margin, and she had *multiple small ecchymoses* (Table II). Blood studies one month later, Jan. 6, 1955, showed hemoglobin 14.7 Gm., erythrocyte count 4.30 million, leukocyte count 5,200, differential count normal, and platelets adequate.

The pregnancy was uneventful and on July 5, 1955, she was delivered of a 6 pound, 10 ounce girl after a 4 hour labor terminated by spontaneous delivery and episiotomy. The puerperium was again uneventful. The *spleen on admission was enlarged to the level of the iliac crest* and *the liver was 3 fingerbreadths below the costal margin.* Blood work on the fourth postpartum day showed hemoglobin 12.6 Gm. (81 per cent), erythrocyte count 3.79 million, and platelets adequate (Table I).

At the examination 6 weeks post partum on Aug. 18, 1955, the uterus was the size of a 6 to 8 weeks' gestation and slightly irregular, the *spleen was palpable at the level of the umbilicus* and the *liver was 3 fingerbreadths below the costal margin.*

When the patient was last seen on April 11, 1956, the *spleen was at the level of the umbilicus* and the *liver 2 fingerbreadths below the costal margin.* Blood studies showed hemoglobin 14 Gm. (91 per cent), erythrocyte count 4.51 million, leukocyte count 6,600, platelets 112,000, and differential count normal. The pelvic findings, aside from the small fibroid uterus, were essentially normal.

Summary

We have presented this case of Gaucher's disease complicating pregnancy because review of the available literature provides little guidance in the management of this problem.

We feel that our experience with this case may be of some value in substantiating the belief that the prognosis for a successful outcome of pregnancy and delivery may be good, despite the presence of Gaucher's disease.

References

1. Whitby, L. E. H., and Britton, C. J. C.: Disorders of the Blood, ed. 5, Philadelphia, 1946, The Blakiston Company.
2. Cecil, Russell L., McDermott, Walsh, and Wolff, Harold G., editors: Textbook of Medicine, ed. 7, Philadephia, 1947, W. B. Saunders Company.
3. Reich, C., Seife, M., and Kessler, B. J.: Medicine **30**: 1, 1951.
4. McElin, T. W., and Mussey, R. D.: Internat. Abstr. Surg. **91**: 105, 1950.
5. Ottenstein, B., Schmidt, G., and Thannhauser, S. J.: Blood **3**: 1250, 1948.
6. Green, J.: Blood **3**: 1238, 1948.
7. Logan, V. W.: Surg., Gynec. & Obst. **72**: 807, 1941.
8. Elliott, J. F.: Canad. M. A. J. **66**: 166, 1952.
9. Bromberg, Y. M., Toaff, R., and Diengott, D.: Brit. M. J. **2**: 761, 1953.
10. Logan, W. P.: J. Florida M. A. **40**: 5, 1953.
11. Gordon, W. H., and Kaufman, J. M.: J. Michigan M. Soc. **49**: 785, 1950.
12. Gelin, G.: Algérie méd. **58**: 209, 1954.

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Reviews and Abstracts

EDITED BY LOUIS M. HELLMAN, M.D.

SELECTED ABSTRACTS*

The Lancet

Volume 1, May 25, 1957.

*Hadfield, G.: The Nature and Origin of the Mammotrophic Agent Present in Human Female Urine, p. 1058.

Hadfield: Nature and Origin of Mammotrophic Agent Present in Human Female Urine, p. 1058.

By the use of hypophysectomized weanling mice as indicators, the following conclusions were reached after 5 experiments: (1) The mammary glands of the weanling male mouse are totally hormone dependent. (2) The ovarian hormones, estrone and progesterone, do not induce any proliferation of the mammary epithelium in this species. (3) Pituitary prolactin alone is also ineffective. (4) Estrone, progesterone, and pituitary prolactin administered together produce a vigorous response at all dose levels. Though the prolactin used may have been contaminated with growth hormone, that the latter had an effect seemed improbable because of the substantial response that was obtained at the lowest dose level when the amount of any contaminating growth hormone must have been quite small. Also, in none of these animals was there any increase in weight at the tenth postoperative day. (5) The urine of premenopausal women can be substituted for the prolactin component of the mammogenic triad. Using this effect in hypophysectomized male weanling mice, a method for the bioassay of prolactin in human urine is available, and it is suggested that an estimation of urinary prolactin may materially assist in the selection of patients with metastatic breast cancer who are likely to benefit from hypophysectomy. The concentration of pituitary prolactin in human female urine was found to vary from 0.01 to 0.25 I.U. per milliliter.

DAVID M. KYDD

Lille chirurgical

Vol. 11, November-December, 1956.

*Gautier, P., Godefroy-Vendeville, Y, and Guiot, Y.: Thecal Tumor of the Ovary, p. 282.

Gautier, Godefroy-Vendeville, and Guiot: Thecal Tumor of the Ovary, p. 282.

A case of proved thecoma of the ovary is presented with a short review of the current literature. The authors note that since 1932 only 300 cases have been reported. A careful

*Titles preceded by an asterisk are abstracted below.

differential diagnosis must be made with that of ovarian fibroma. Thecoma is most often associated with hyperplasia of the endometrium. Malignancy is rare and usually only observed after the age of 50.

ROBERT C. KNAPP

The Medical Journal of Australia

Vol. 1, April 20, 1957.

*Poidevin, L. O. S.: Some Childbirth Customs Among the Ngalia Tribe, Central Australia, p. 543.

Poidevin: Some Childbirth Customs Among the Ngalia Tribe, Central Australia, p. 543.

This secondhand report concerns itself with the births of two Australian aborigines in the Ngalia tribe of Central Australia near the Yuendumu Native Settlement.

As explained by the author, these births were not actually witnessed, but several anecdotal features were mentioned. Of interest is the fact that "the newborn pickaninnies" of this tribe are slowly decreasing. In 1953 there were 29 newborn infants as compared to 19 in 1955. The actual delivery apparently is performed in the squatting position and the colored granny midwife applies ashes and force to the fundus at the height of contractions. The husband is out of earshot during the proceedings. Early ambulation and the squatting over a smoke fire serve for puerperal care.

A. STARK WOLKOFF

Die Medizinische

Vol. 1957, No. 23, June 8, 1957.

*Schmidt, W.: The Effects of a New Spasmolytic Agent—Epidosin—in Obstertics, p. 870.

Schmidt: The Effects of a New Spasmolytic Agent—Epidosin—in Obstetrics, p. 870.

The author reports on the use of Epidosin (phenylmethylvaleriaacid-beta-diethylaminoethylester-bromethylate) a new spasmolytic agent which acts directly on the musculature like papaverine and also blocks parasympathetic action on smooth muscle like atropine. The medications were given in the form of suppositories and also combined with injections or as injections alone. The suppositories contain 20 mg. and the ampules 8 mg. The drug was given to 264 women (141 primigravidas and 123 multiparas) ranging in age from less than 20 years to more than 35 years, although 169 of them fell into the 21 to 30 year group. No specific time studies are presented by the author but several case reports are listed to bear out the point that labor is markedly accelerated by this drug and that at the same time it has no harmful action on the mother or child.

FRANCIS B. O'BRIEN

Vol. 1957, No. 24, June 15, 1957.

*Nowc, A.: Relief of Puerperal Urinary Retention, p. 916.

Nowc: Relief of Puerperal Urinary Retention, p. 916.

A drug called Dismenol is used, which previously had been used for dysmenorrhea, for relieving puerperal urinary retention. This drug is composed of parasulfaminobenzoic-acid and dimenthylaminophenazone and comes in tablet form. In a group of 358 puerperal patients it was necessary to treat 50. Twenty-two of these women could empty the bladder spontaneously after one tablet. Thirteen were relieved after 2 tablets were given twice. The remaining 15 patients did not respond and had to be treated by catheterization and other methods. The author feels that in 70 per cent of the cases of puerperal urinary retention the patient can be relieved easily and without side effects and can obtain relief of the after-birth pains to a great degree.

FRANCIS B. O'BRIEN

New England Journal of Medicine

Vol. 255, December 13, 1956.

*Gryboski, W. A., and Spiro, H. M.: The Effect of Pregnancy on Gastric Secretion, p. 1131.

Gryboski and Spiro: Effect of Pregnancy on Gastric Secretion, p. 1131.

The authors used the indirect measure of gastric secretion by the blood pepsin method to study the effect of pregnancy on gastric secretion in an attempt to evaluate the clinical impression that pregnancy may alleviate the symptoms of peptic ulcer. Blood pepsin levels parallel gastric pepsin levels, and so can be taken as a reflection of gastric secretory activity. The authors' study indicates that the mean values in the first six months of pregnancy show no significant variation from the normal. A rise in the mean blood pepsin values was observed during the third trimester, and the levels reached a peak on the day after delivery, falling to normal values by approximately 120 days post partum. The rise in blood pepsin during the last trimester suggests an increase in gastric secretion, and the authors point out that these observations suggest that there are data which cast doubt on the clinical impression that the symptoms of peptic ulcer are ameliorated during pregnancy.

DOUGLAS M. HAYNES

Vol. 255, December 20, 1956.

*Jackson, W. P., and Woolf, N.: The Natural History of Prediabetes, p. 1183.

Jackson and Woolf: The Natural History of Prediabetes, p. 1183.

The authors present the case history of a typical so-called "prediabetic" patient. This woman, whose mother was diabetic, experienced progressive increase in weight, and there was progressive increase in the weights of successive babies born to her. Her eighth baby was stillborn; her ninth was premature and died neonatally; at autopsy there were grossly enlarged islands of Langerhans in this infant's pancreas, and the liver showed extramedullary hemotopoiesis. The authors saw the patient in her tenth pregnancy, and performed a glucose tolerance test at 8 months' gestation which showed an elevation of the blood sugar levels at 2 hours and 2½ hours. Cesarean section was performed before term with delivery of an edematous infant who weighed 13 pounds. In the puerperium the patient's glucose tolerance curve reverted to normal, but on being retested some months later it was again abnormal in a prediabetic manner. Two years later the patient had gross glycosuria and a true diabetic tolerance curve. The authors point out that prediabetes should be suspected as the cause of any unexplained stillbirth and tested for by determination of glucose tolerance and examination of the pancreas of the infant. The authors point out that it is strange that, by examining the tissues of her child, one may consistently make the diagnosis of a disease which may not be manifest for years in the mother.

DOUGLAS M. HAYNES

Vol. 256, January 24, 1957.

*Creger, W. P., and Steele, M. R.: Human Fetomaternal Passage of Erythrocytes, p. 158.

Creger and Steele: Human Fetomaternal Passage of Erythrocytes, p. 158.

The authors' studies were designed to test the hypothesis that appreciable numbers of fetal red cells gain entrance to the maternal circulation in normal pregnancy. The rationale of their method was as follows: If the mother and the fetus are of different ABO groups, fetal red cells that may have gained entrance to the maternal circulation can be counted separately from the mother's erythrocytes by means of antigenic differences in the two sets of cells. With mothers of group A and infants of group O, a count was made of agglutinated red cells left in the maternal blood specimen after maximal agglutination by

anti-A blood grouping serum. The authors assume that these unagglutinated cells were composed of maternal unagglutinated cells and any fetal cells of group O which might be present. A second maternal sample was obtained six weeks post partum and the unagglutinated cell count was repeated. The assumption was made that the fetal red cells would have disappeared, resulting in decline in the total count of unagglutinated cells. A control group composed of group A mothers before and after delivery of group A babies was similarly studied. The average unagglutinated red count of 14 mothers in group A who bore group O infants was higher at delivery and showed a significantly greater decline six weeks post partum than that of 9 group A mothers who bore group A infants. The authors suggest that this finding implies the presence of fetal erythrocytes in the maternal circulation in normal pregnancy, and furnishes indirect evidence that vigorous maternal antibody-forming ability in the pathogenesis of erythroblastosis fetalis is a function of transplacental erythrocyte migration.

DOUGLAS M. HAYNES

Vol. 256, February 28, 1957.

*Jewett, John Figgis: Changing Maternal Mortality in Massachusetts, p. 395.

Jewett: Changing Maternal Mortality in Massachusetts, p. 395.

The author reviews statistical data on maternal mortality in the remote past in England and France and recently in Massachusetts. In 1955, the primary avoidable factors were inadequate prenatal care in 38 per cent, delay in 19 per cent, and surgical error in 19 per cent. The surgical errors were all associated with cesarean section, in itself associated with 27 per cent of all maternal deaths. The most disturbing cause or contributing cause of death was sepsis, and the author points out that it can be assumed that this always occurs from a break in technique unless the contrary is proved. The author decries the indiscriminate use of so-called prophylactic antibiotics, which destroy the suspectible organisms, leaving a clear field for the more virulent ones, and provide a false sense of security. He concludes that a study of the current most common primary avoidable factors in maternal mortality stresses five imperative demands upon the profession: both physicians and the public must be educated to realize the importance of better prenatal care; instantaneous transfusion facilities must be available in hospitals in which obstetrics is performed; cesarean section should be avoided unless strictly indicated; more rigorous attention to asepsis should be resumed to combat the rising proportion of deaths from sepsis; and obstetricians must demand better anesthesia.

DOUGLAS M. HAYNES

Wiener klinische Wochenschrift

Vol. 68, September 14, 1956.

*Weiss, H., and Strametz, R.: Concerning Alterations in the Excretory Urinary Passages in Parametritis, p. 720.

Weiss and Strametz: Concerning Alterations in the Excretory Urinary Passages in Parametritis, p. 720.

In the clinical syndrome of acute parametritis, the serious clinical manifestations of the acute disease are predominant, so that the frequent urinary complications in the excretory urinary passages are often overlooked. In 33.3 per cent of all cases of either unilateral or bilateral parametritis observed by the authors in the University Gynecologic clinic in Graz, urinary tract alterations of both anatomical and functional type were diagnosed. The etiology of these alterations was thought to be both toxic and mechanical in origin. Follow-up studies showed that most of this urinary tract damage was of a reversible type. The authors emphasize the need for further clinical studies in a larger group of patients.

DOUGLAS M. HAYNES

Vol. 68, November 23, 1956.

*Elsner, P., and Thewanger, W.: New Points of View in the Treatment of Puerperal Mastitis, p. 930.

Elsner and Thewanger: New Points of View in the Treatment of Puerperal Mastitis, p. 930.

The authors point out by statistical data that the incidence of puerperal mastitis has definitely increased during the past several years, notably during the antibiotic era. The authors present clinical data on 324 patients with the diagnosis of puerperal mastitis observed over a period of 12 years. These patients are analyzed in three separate categories: those treated by conservative methods such as heat, diathermy, binding of the breasts; those with conservative therapy supplemented by sulfonamides; and those treated with antibiotics, chiefly penicillin. Ninety-three per cent of the mastitides were proved to be due to *Staphylococcus aureus,* the remainder being either *Escherichia coli* or pyocyaneus infections. Eighty-four per cent of all patients with staphylococcal infections showed resistance to penicillin. A startling increase in the over-all morbidity from mastitis in the years 1953, 1954, 1955 is interpreted by the authors in the light of an increased number of infections with penicillin-resistant organisms consequent to the indiscriminate use of antibiotics. Although organismal resistance to broad-spectrum antibiotics was low, the authors believe that the use of the conservative nonantibiotic therapy of mastitis is preferable, as the use of the antibiotics not only produces resistant strains of organisms, but fails to control a well-established infection efficiently, and demonstrably increases the time required for resolution of the inflammatory process.

DOUGLAS M. HAYNES

Vol. 68, November 30, 1956.

*Froewis, W., Michalica, W., and Spurny, J.: Results of Operations for Prolapse—A Ten Year Report, p. 947.

Froewis, Michalica, and Spurny: Results of Operations for Prolapse, p. 947.

The authors report the clinical results in 305 patients operated upon for partial and total genital prolapse during the period 1945-1954 in the First University Gynecologic Clinic of Vienna. Of the 305 patients, only 125 were available for adequate follow-up. The primary mortality was 0.7 per cent; 83.2 per cent of the patients were completely healed. Asymptomatic recurrences occurred in 7.2 per cent, and symptomatic recurrences in 9.6 per cent. Ten different operative procedures were used, including the Manchester operation and the Watkins-Wertheim interposition operation. In appropriate cases, the authors favor the use of a colpocleisis over vaginal plastic repair. Of interest to American gynecologists will be the fact that vaginal hysterectomy associated with plastic vaginal repair was done in only 10 patients.

DOUGLAS M. HAYNES

Vol. 69, February 8, 1957.

*Halter, G.: The Condition of the Endometrium Following Ampuation of the Portio, p. 100.

Halter: Condition of the Endometrium Following Amputation of the Portio, p. 100.

The author reviews 150 cases of surgical procedures involving amputation of the cervix. He found that in the overwhelming majority of cases there were no alterations in the menstrual cycle of patients who had had amputation of the portio. Although review of the literature suggested that chronic endometritis might result from these operations, the present series did not bear this out. The series included 46 women under the age of 40, 7 of whom became pregnant and 3 of whom who were subsequently delivered at term. Complications secondary to surgical stenosis were encountered 17 times in the series. From

his experience, the author concludes that there is no clinically significant danger of endometrial infection following amputation of the cervix, nor is stenosis an important problem when proper trachelorrhaphy procedures are followed. On the other hand, he believes that the procedure should not be performed frequently in women in the childbearing years because of the possibility of weakening of the internal os and interference with subsequent pregnancies.

DOUGLAS M. HAYNES

Vol. 69, February 22, 1957.

*Elsner, P., and Kaiser, E.: Concerning the Significance of the Occurrence of Lysozyme in the Female Genital Tract, p. 138.

Elsner and Kaiser: Significance of the Occurrence of Lysozyme in the Female Genital Tract, p. 138.

The authors review the properties of the enzyme lysozyme and report a series of investigations into the occurrence of lysozyme in the female genital tract. It was possible to demonstrate the enzyme in both vaginal and cervical secretions, and the authors' researches indicate that the presence of the enzyme depends largely on the number of polymorphonuclear leukocytes present, and it is present in largest quantity when the leukocytes are degenerating. These results suggest that lysozyme plays very little part in the preservation of the relatively sparse bacterial flora of the female genital tract.

DOUGLAS M. HAYNES

Vol. 69, March 8, 1957.

*Lorant, P.: Ten Cases of Measles in Pregnancy, p. 171.

Lorant: Ten Cases of Measles in Pregnancy, p. 171.

Ten women from Vienna and southern Austria were traced who during the years 1940 to 1950 had clinical attacks of German measles during pregnancy. Only 6 of these had the disease in the first trimester. There were 2 abortions, 2 premature infants who survived, and 5 normal infants delivered at term in the series; the only congenital anomaly observed was in the infant of the patient who had the disease in the first month of pregnancy. This infant had a cleft palate and died two months after delivery. No other congenital anomalies were encountered at autopsy. The author is obviously unable to draw any general conclusions from these meager data, which are the first reported from Austria.

DOUGLAS M. HAYNES

Vol. 69, March 15, 1957.

*Weghaupt, K.: Hormonal Therapy of Female Genital Carcinoma, p. 181.

Weghaupt: Hormonal Therapy of Female Genital Carcinoma, p. 181.

Although the mechanism of contrasexual hormones in breast and prostate cancer is fairly well understood, in the case of female genital carcinoma it is relatively controversial. The author quotes the work of Limburg in which it was demonstrated by smear techniques that in patients in the advanced menopause in whom no estrogenic effect was seen in repeated vaginal smears, the incidence of carcinoma of the corpus or the breast was extremely low, but carcinoma of the cervix still had an appreciable incidence. Two groups of genital carcinoma are recognized: the so-called "irritative" cancers (vulvar, vaginal, and portio carcinoma); and the so-called "systemic" cancers (corpus, tube, and ovarian cancer). The literature is reviewed extensively, and stress is placed on the anabolic and mood-elevating effect of antigenic hormone therapy in patients with genital carcinoma. The author emphasizes that although this method of treatment is palliative in many cases, no curative effect has ever been demonstrated.

DOUGLAS M. HAYNES

Zentralblatt für Gynäkologie

Vol. 79, February 2, 1957.

*Kraussold, E.: "Elective" Therapy of Carcinoma of the Cervix—Statistics from the University of Berlin 1949-50 and Cumulative Statistics 1910-50, p. 169.

Kraussold: "Elective" Therapy of Carcinoma of the Cervix, p. 169.

"Elective" therapy for carcinoma of the cervix is a term coined by Stoeckel for radiation and surgical treatment of this disease in combination or for either treatment alone. This paper gives local statistics for 1949 to 1950 and national (German) statistics from 1910 to 1950.

In the recent 2 year period, 449 cases were discovered with an over-all 5 year cure rate of 39 per cent (176 patients). Fifty per cent of the patients were in Stage I or II. Twelve of the patients had carcinoma of the cervical stump with only a 25 per cent cure rate. No follow-up was available in 5 per cent of the patients. Correcting for this, the cure rate rises from 39 to 41 per cent. Two hundred and eighty-nine patients, or 64 per cent of cases in all stages, underwent operation followed by radiation. Five year cures were obtained in 58 per cent of the Stage I cases, 54 per cent of Stage II, 26 per cent of Stage III, and 47 per cent of Stage IV. The operative mortality was 5 per cent. One hundred fifty-one patients received irradiation alone, with 5 year cures of 47 per cent in Stage I, 44 per cent in Stage II, and 21 per cent in Stage III. There was a primary mortality of 1.3 per cent, with an over-all radiation cure rate of 27.5 per cent. The breakdown by operations is:

Radical vaginal hysterectomy:	266 patients in Stages I, II and III, with 3.7% surgical mortality and 48% cure rate
Radical abdominal hysterectomy:	13 patients in all stages with 15% surgical mortality and 54% cure rate
Vaginal hysterectomy:	10 patients in Stage I with 10% surgical mortality and 10% cure rate

The figures from all of Germany from 1910 to 1950 given for comparison are:

All cases	6,949		
Stages I and II	3,757	(54%)	
Operated upon—all stages	2,515	(36%)	
5 year cure	2,199	(32%)	No follow-up in 612 patients, giving a corrected rate of 35%
5 year cure in Stages III and IV		(16%)	
Primary mortality:			
Surgical	206	(8%)	
Radiation	100	(2%)	
Total	306	(4.4%)	
Supportive treatment only	135	(2%)	

WALTER F. TAUBER

Vol. 79, March 2, 1957.

*Kucera, Fr.: The Histogenesis of Carcinoma of the Body of the Uterus, p. 347.

Kucera: Histogenesis of Carcinoma of the Body of the Uterus, p. 347.

Glandular hyperplasia of the endometrium is found to be followed by carcinoma in 3 per cent of the patients of childbearing age but in 25 per cent after the menopause. Six hundred seventy-one uteri were examined after hysterectomy, showing that there is a difference pathologically between the pre- and postmenopausal uteri. Hyperplasia during the childbearing age is found in the functional layer. Later it is found in the basal layer.

WALTER F. TAUBER

Items

Second World Congress of Gynecology and Obstetrics

The International Federation of Gynecology and Obstetrics, founded in Geneva in 1954, will hold its Second World Congress in Montreal from June 22 to June 28, 1958.

All scientific sessions, scientific exhibits, and moving pictures will be held in the newly built Queen Elizabeth Hotel. The main features will be plenary conferences with invited guest speakers, round table discussions, and free communications.

Information and registration forms may be obtained by writing to the Montreal Committee, Second World Congress, International Federation of Gynecology and Obstetrics, 1414 Drummond Street, Suite 220, Montreal 25, Quebec, Canada.

American Board of Obstetrics and Gynecology

The Part I Examinations of the American Board of Obstetrics and Gynecology are to be held in various parts of the United States and Canada on Thursday, Jan. 2, 1958, at 2:00 P.M.

Candidates notified of their eligibility to participate in Part I must submit their case abstracts within thirty days of notification of eligibility. No candidate may take the Written Examination unless the case abstracts have been received in the office of the Secretary. Candidates resubmitting cases must send them in by Nov. 1, 1957.

Current Bulletins outlining present requirements may be obtained by writing to the Secretary's office.

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American Journal of OBSTETRICS AND GYNECOLOGY

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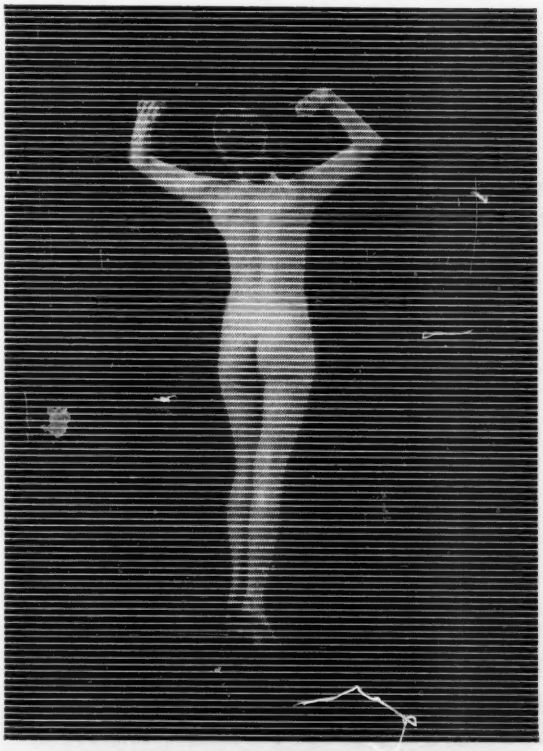

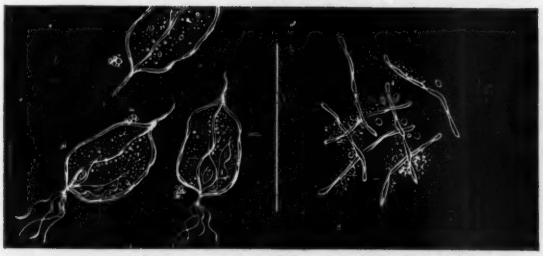

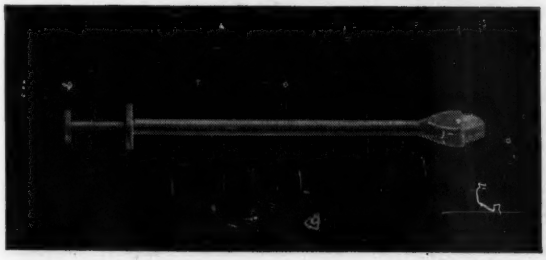

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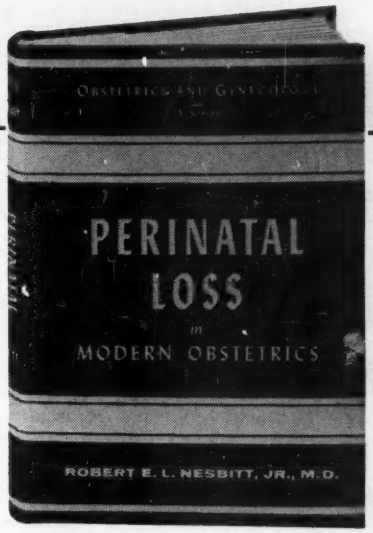

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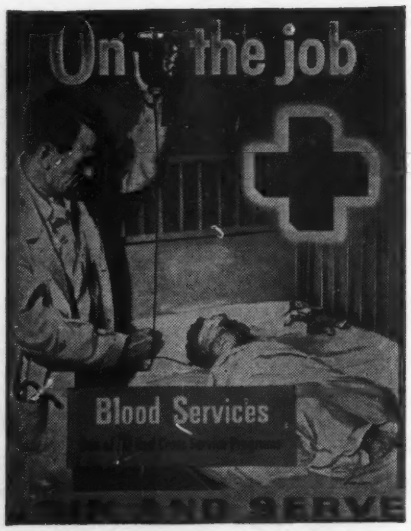

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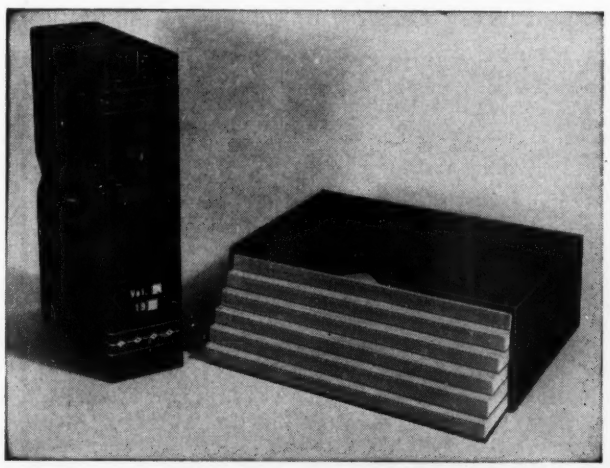

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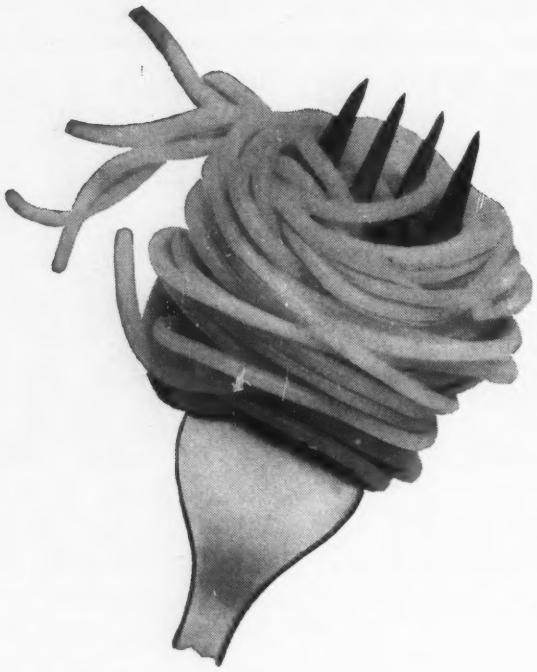

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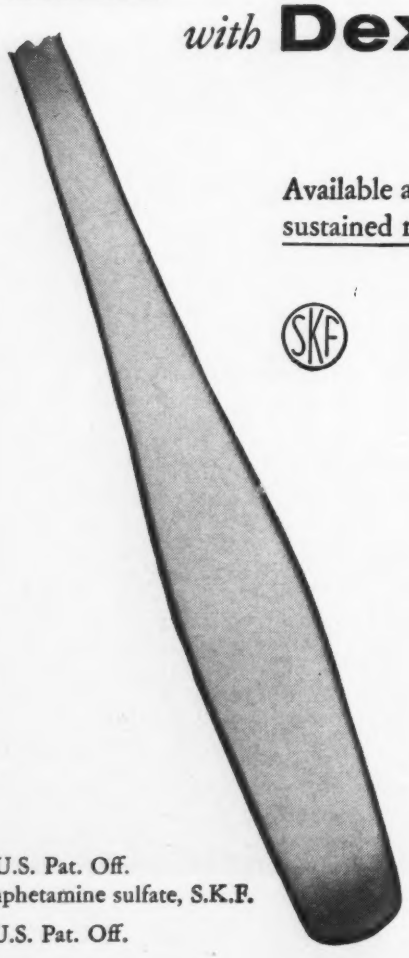

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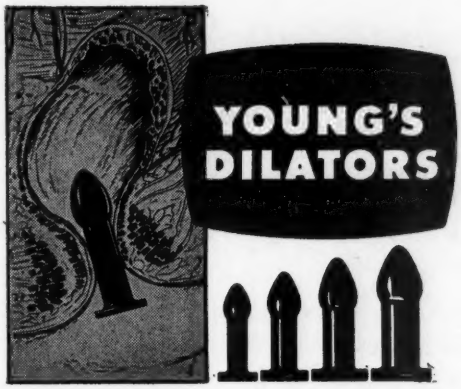

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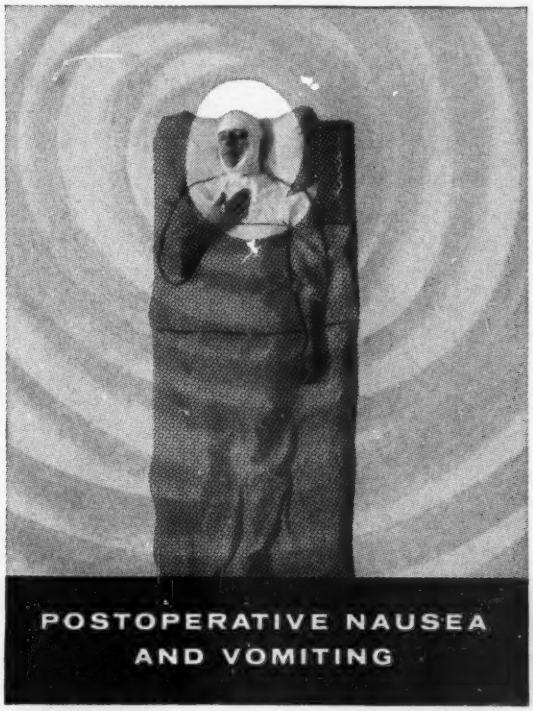

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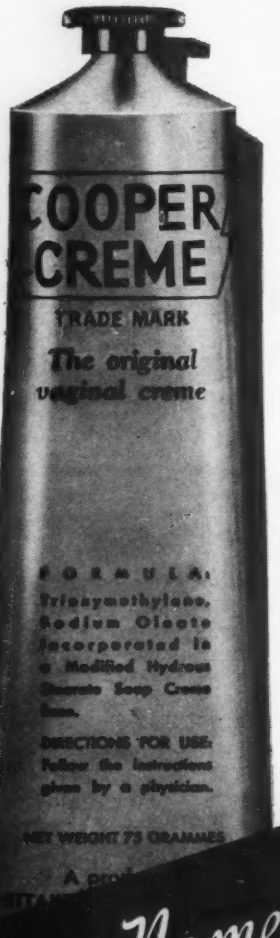

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